

## Antimicrobial residues in foods of animal origin in Africa: public health risks

This paper (No. 10062014-00034-FR) has been peer-reviewed, accepted, edited, and corrected by authors. It has not yet been formatted for printing. It will be published in December 2014 in issue 33-3 of the *Scientific and Technical Review*

S.E.P. Mensah <sup>(1)\*</sup>, O.D. Koudandé <sup>(1)</sup>, P. Sanders <sup>(2)</sup>, M. Laurentie <sup>(2)</sup>, G.A. Mensah <sup>(1)</sup> & F.A. Abiola <sup>(3)</sup>

(1) Institut National des Recherches Agricoles du Bénin, Centre de Recherches Agricoles d'Agonkanmey, Laboratoire des Recherches Zootechnique, Vétérinaire et Halieutique (INRAB/CRA-Agonkanmey/LRZVH), 01 BP 884 Recette Principale, Cotonou, Bénin

(2) Agence Nationale de Sécurité Sanitaire (ANSES), Laboratoire de Fougères, 35302 Fougères Cedex, France

(3) Université d'Abomey-Calavi, Faculté des Sciences et Techniques (FAST/UAC), 01 BP 2009, Cotonou, Bénin

\*Corresponding author: egidemensah@yahoo.fr

### Summary

The authors report on the current status of work on residues of veterinary medicinal products and, in particular, antimicrobial residues in foods of animal origin. This review focuses on residues of veterinary antimicrobials, antimicrobials used in livestock production, the concept of residues, and antimicrobial residues in foods of animal origin. Only one antimicrobial substance has been approved in the West African Economic and Monetary Union, compared with 16 substances in Benin and 56 in the European Union. The issue of antimicrobial residues in foods of animal origin has rarely been a serious concern in developing countries, in contrast to the situation in Europe. However, while the prevalence of veterinary drug residues in foods of animal origin is less than 1% in Europe, in some African

countries it can be as high as 94%. Antimicrobial residues in foods of animal origin can cause allergies, cancer, alterations in the intestinal flora, bacterial resistance and the inhibition of fermentation in the dairy industry. The harmonisation of regulations in Africa could reduce the circulation of prohibited antimicrobials and lead to the implementation of a plan for the control and surveillance of residues from veterinary medicinal products in foods of animal origin.

### **Keywords**

Africa – Antimicrobial residues – Antimicrobials – Foods of animal origin.

### **Introduction**

The intensification of animal production in recent decades has been aided by the use of veterinary medicinal products; in particular, anti-infective drugs in modern livestock production (1, 2). These medicinal products are used either as a curative treatment, applied individually or collectively to animals with microbial infections, or as a preventive treatment against the onset of certain diseases, or even, in extreme cases, to offset poor animal production hygiene (3). The use of anti-infectives as medicine is a very recent development and is seen as one of the biggest medical breakthroughs because it can dramatically reduce the morbidity and mortality caused by many bacterial infectious diseases (4). However, it alters the ecology of bacteria and contributes to the selection of resistant strains (5).

After their administration to animals, such treatments leave residues in the tissues of these animals and the foods derived from them (6). The presence of antimicrobial residues in foods of animal origin, combined with failure to comply with the instructions for their use (dosage and waiting period) or poor livestock production practices, can have serious consequences for consumer health (7, 8).

The regulations for veterinary pharmaceuticals define an *a priori* risk assessment procedure to evaluate their active ingredients and set maximum residue limits (MRLs). In the subsequent assessment for

marketing authorisation for each medicinal formulation, a waiting period between the latest administration of the product and the marketing of food from the treated animals is defined for the authorised dosage. Finally, management recommendations for their use (good veterinary practices, animal identification, veterinary prescription, a waiting period, a livestock register) are provided to reduce risk.

To penetrate the globalised international market, agriculture in developing countries must offer products that are competitive in terms of quality and quantity. Thus, the establishment of a standardisation and quality assurance framework, to enhance the production and food safety environment of businesses and avoid the presence of products harmful to human and animal health, is a prerequisite for the development of sustainable livestock production (9). Indeed, sustainable livestock systems in developing countries must meet the demand for animal products without compromising people's future nutritional needs or damaging the environment. We need to analyse how the potential of small farms can be harnessed by intensification, in line with the type of animal production employed and changing economic circumstances. Feeding and management methods aimed at boosting productivity and mitigating negative environmental impacts must be addressed in a realistic and practical manner. All this is taking place in an evolving context of market demand, production and technological efficiency that places a premium on innovative approaches and practices, including institutional, political and commercial solutions, implemented chiefly in a 'value chain' context (10).

Current developments in the market economy are prompting the liberalisation of the veterinary profession. The problem is that, in most African countries, there is no control over the distribution of veterinary pharmaceuticals and phytosanitary products. Worse still, no appropriate legislation yet exists to guarantee the quality of the various products released onto the African market (11).

In addition to the health risk to local populations, the presence of residues from veterinary medicinal products in foods of animal origin could jeopardise international trade in the wake of the World Trade Organization (WTO) Agreement on the Application of Sanitary and Phytosanitary Measures (the ‘SPS Agreement’), which underpins the globalisation of markets, and of agreements by the West African Economic and Monetary Union (UEMOA) governing the West African market. Compliance with the Codex Alimentarius Commission rules on veterinary drug residues should serve as a guarantee of quality, enabling African livestock producers to access other markets.

This literature review examines the scientific and regulatory context of veterinary drugs; the antimicrobials available for use as veterinary products in Africa; drug residues; international and African legislation on residues; risk factors associated with antimicrobial residues in foods of animal origin; and residue control plans.

## **Background**

A whole series of known or new foodborne biological and chemical hazards are threatening health (12). In the European Union (EU), following a string of health crises, the food safety mechanism has evolved towards a risk analysis approach. This shift to the concept of ‘farm to fork’ risk management (13) led to the establishment of food safety agencies at the European level. The risks of residues from veterinary medicinal products used in livestock production were taken on board in the 1980s, most notably through European harmonisation of the regulations on medicinal products for veterinary use. Over the past decade, the EU has improved its regulatory framework to better supervise, assess, monitor and control food production under the ‘Food Law’. More recently, the use of anti-infectives in livestock and its contribution to the development of antimicrobial resistance has attracted considerable attention, with the introduction of community and national surveillance programmes for zoonotic bacteria (14). In Africa – particularly West Africa – only microbial pathogens, pesticide residues and aflatoxins have been the subject of measures to

protect the safety of food for human consumption. These hazards were perceived as the greatest threat to public health. In April 2007, the eight UEMOA countries (Benin, Burkina-Faso, Côte d'Ivoire, Guinea-Bissau, Mali, Niger, Senegal and Togo) adopted regulation 07/2007/CM/UEMOA concerning plant, animal and food safety in the UEMOA area (15). More recently, in 2010 and 2011, two training sessions were held in Benin to familiarise these countries with the theoretical framework for health risk analysis (16, 17). While UEMOA still has no functioning system to detect residues from veterinary medicinal products in foods of animal origin, the experts responsible for approving marketing authorisation applications are keeping a watchful eye on waiting times, in order to minimise medicinal residues in food. As yet, there have been very few studies on antimicrobial residues affecting food safety (9). However, in developing countries, failure to respect waiting periods (7) leads to high exposure to antimicrobial residues (18).

## **Use of antimicrobials in livestock production**

### **Antimicrobials as growth factors**

Growth promoters are antimicrobials which, when administered in low doses in animal feed, have a preventive effect against certain bacterial infections and modify the composition of the intestinal microbiota, improving feed assimilation. The impact of these protective effects on animal production is to accelerate livestock growth (3). In the interests of consumer protection, European marketing authorisation bodies determined that the animal production benefits of additives in livestock feed failed to justify such use because the risk of the selection of resistant bacteria could have a disastrous impact on public health. Nevertheless, in the United States, a large number of antimicrobials are still authorised for use in low doses as growth factors (3). In the EU, only ionophoric antimicrobials (monensin, narasin, salinomycin and lasalocid A) are still authorised as coccidiostats and as additives in animal feed (19).

## **Veterinary antimicrobials**

Antimicrobials are the main group of veterinary medicinal products used since the 1950s to treat bacterial infectious diseases in both food-producing and companion animals. The substances used belong to the same families as those used in human medicine (4). These medicinal products are administered to prevent and treat infectious diseases that could cause significant morbidity and possible mortality. The most commonly treated disorders are digestive and respiratory (20). For several types of integrated farm systems where animals (poultry, pigs, calves and fish) are raised in groups indoors, production conditions prompt veterinarians to prescribe these treatments for both preventive and curative purposes. For other production systems, treatments are individual and mostly curative.

The three types of veterinary treatment (4) are: preventive treatment (prophylaxis), administered at a time in the animal's life when the risk of bacterial infection is considered to be very high; curative treatment administered to sick animals; and control treatment (metaphylaxis) prescribed for groups of animals in contact with sick animals (21).

### **Authorised veterinary antimicrobials**

In the EU, the antimicrobials approved for use as veterinary drugs figure in the list of substances in Annex 1 of Commission Regulation (EU) 37/2010 (22). The medicinal products containing these antimicrobials authorised for veterinary use are those that have passed the marketing authorisation process of the competent national or European authority. After an evaluation of the scientific data proving the efficacy of the product and its safety for humans, animals and the environment, the Competent Authority authorises its importation, distribution and use (11).

The statutory marketing authorisation mechanism is virtually identical across most African countries. No medicinal product may be marketed unless it has first been authorised by the Competent Authority. However, there are huge shortcomings in the implementation because the technical evaluation of a marketing application is limited to an

administrative procedure alone. These countries have no effective scientific control tools to ensure the validity of the data provided by the applicant. In addition, the procedures do not cover all veterinary specialities marketed in these countries (11). In the UEMOA region, the accreditation system for veterinary medicinal products was introduced in 2006 but only came into operation in 2010.

The main classes of antibiotics and antimicrobials authorised in the EU, UEMOA and Benin are summarised in Table I.

### Prohibited veterinary antimicrobials

Prohibited antimicrobials are substances for which it is not possible to determine the MRL. These are listed in Annex 2 of European Commission Regulation 37/2010 (22). It should also be borne in mind that antimicrobial substances not listed in Annex 1 of this regulation must not be used in food-producing animals.

Chloramphenicol is a broad-spectrum antimicrobial against Gram-positive and Gram-negative bacteria. While it is an effective therapeutic for a wide range of animal diseases, historic epidemiological data have shown that its use in humans may be associated with haematological disorders; in particular, aplastic anaemia. During its assessment, it was not possible to determine an MRL based on the available data. The inability to set a threshold value and shortcomings in the marketing authorisation application led to chloramphenicol being classified in 1994 as a prohibited substance for use in food-producing animals in the European Community.

Nitrofurans have been banned from use as a veterinary medicinal product and as additives in the EU since 1998.

Dapsone, which is used to treat leprosy in humans, is not authorised for use in food-producing animals in Europe because of insufficient toxicology data, making it impossible to determine the acceptable daily intake (ADI).

## **Use of antimicrobial drugs**

According to EU regulations, antimicrobials and veterinary medicinal products require a veterinary prescription. Drug-dispensing procedures vary from one Member State to another (4).

In sub-Saharan Africa, there are massive shortcomings in the organisation of the veterinary drug market. These include: a lack of specific legislation geared to the recent liberalisation of veterinary pharmaceuticals; failure to enforce current regulations; a lack of veterinary drug inspections, marketing authorisation procedures and registration; and the existence of parallel channels alongside the official distribution channel for veterinary drugs (11). These failings raise a number of questions about the holding, marketing, prescription and quality of veterinary drugs in circulation.

In addition to veterinary drugs imported from the West, products manufactured by laboratories in Africa and Asia, especially those in India and Nigeria, are found on the African market. Nigeria supplies Niger, Cameroon and Benin (11). This makes them high-risk countries for the distribution of hazardous and prohibited veterinary medicinal products. In terms of effectiveness, treatment with such drugs offers no guarantee of a cure for the disorders and deficiencies in question. In terms of safety, the consumption of food from improperly treated animals could have disastrous consequences for both humans and livestock. For this reason, such countries face considerable public health problems.

## **Analysis of usage**

A study of the quality of medicinal products revealed that 48% of those in circulation in Benin and Togo are counterfeit (23). This is supported by surveys in Benin, Togo, Mali, Mauritania, Cameroon and Chad, where almost 61% of medicinal products do not comply with international standards; i.e. do not have genuine regulatory marketing approval (24, 25, 26). Reports from Senegal point to the indiscriminate use of antimicrobials, even prohibited ones, by unqualified personnel on poultry farms in the Niayes region (27).

Benin has had a marketing authorisation procedure for veterinary medicinal products since 2004 (28). A list of veterinary drugs was drawn up and updated in 2011. Surveys of cattle and poultry farms could be used to identify and collect the antimicrobials in circulation; these antimicrobials could then be checked to see whether they conform to those authorised by the EU or UEMOA. A microbiological, physical and chemical analysis of the antimicrobials used in cattle production would serve to assess their quality and conformity with marketing authorisation recommendations, as well as to detect counterfeit drugs. It is also necessary to determine the conditions of antimicrobial use by: quantitatively defining the frequency of use in terms of therapeutic indications; exploring disparities in procedures among farms; and identifying the associated parameters. Antimicrobial use may well be linked to the structure of the farm or livestock production unit, animal health practices or human factors.

## **Residues of medicinal products**

### **Concept of residues**

Residues are defined as all active ingredients or metabolites of those ingredients that remain in meat or other foodstuffs from the animal to which the medicinal product in question has been administered (29). Regulation No. 470/2009 of the European Parliament and of the Council defines residues as all pharmacologically active substances, whether active ingredients, excipients or degradation products, and their metabolites, which remain in animal-derived food.

The concept of drug residues in food was developed over the second half of the 20th Century, resulting in the definition of a 'no observed effect' level, an ADI and an MRL in food (30). This reflected advances in our knowledge of toxicological risk assessment and analytical science in the field of pharmacokinetics (Fig. 1).

For most antimicrobials and anti-infectives, the results of microbiological studies are used to determine the maximum dose that

has no observed effect. For a few other substances, there is a toxic risk (Table II).

Studies to compare the absorption, distribution, metabolism and elimination in laboratory and target animals are used as the basis for studying the kinetics of total residues, the extractable fraction compared with the bound fraction, the nature of metabolites and their main effects. These data are used to define the marker residue (parent substance, metabolite or combination of substances) whose depletion from the tissue is correlated with that of total residues. The MRL in various foodstuffs (muscle, liver, kidney, fat, milk and eggs) is determined to minimise the risk of consumer exposure, taking into account dietary intake. Such considerations as food technology, good farming practices and the use of veterinary medicinal products may also be taken into account when setting the MRL.

### **Residue control methods**

In the EU, self-monitoring and the control of residues are based on standardised analytical methods. Much of this analysis is carried out in the laboratory. The regulatory framework in force in the EU is based on Directive 96/23/EC, which structures the network of laboratories approved for official residue control, laying down requirements in terms of quality and performance of analytical methods (Decision 2002/657) (32). This framework has contributed to the harmonisation of controls.

Conversely, in UEMOA countries, the list of references of harmonised analysis methods for food did not include any methods for analysing veterinary medicinal products. Analysis methods vary from one country to the next, and even among laboratories, because of the lack of UEMOA-accredited methods. Against a background of trade globalisation, analysis methods must be standardised and applied by all laboratories, with equivalent levels of performance.

In general, the residue control strategy is based on a two-step approach: the detection of residues using sensitive tests with a low rate of false negatives; followed by confirmation, requiring

quantification against the MRL and identification with a low rate of false positives.

### Detection methods

The methods most often used to detect antimicrobial residues in food obtained from animals are the official methods, which often depend on the matrix. Microbiological and immunological methods are used to detect antimicrobial residues in milk and muscle. Two types of microbiological test are employed: one using test tubes (Delvotest/DSM, Charm I/Charm II, Eclipse/Zeu-Inmunotech) and the other using combinations of Petri dishes (33). Immunological techniques, such as enzyme-linked immunosorbent assay (ELISA), radioimmunoassay, and receptor binding are also used with different instruments for measurement (34, 35).

### Confirmation methods

Samples testing positive are analysed using various physical and chemical confirmation techniques, such as liquid chromatography-UV detection and fluorimetry, or combined with mass spectrometry. These methods are designed to satisfy a number of performance criteria, which are verified during the required validation studies before being used for statutory control, in accordance with Decision 2002/657/EC (32, 36).

Several physical/chemical confirmation methods have been developed (37, 38, 39, 40, 41).

### **Antimicrobial residue risk factors associated with poor practices**

The therapeutic arsenal offered by the pharmaceutical industry, combined with the growing use of antiparasitics and antimicrobials to prevent and treat diseases, increases the probability of residues of these substances in products obtained from animals (42). The factors favouring the presence of antimicrobial residues in foods of animal origin include: failure to comply with the waiting period after the administration of antimicrobials; failure to consult a veterinarian

before using antimicrobials; lack of prior training in animal husbandry; and the type of livestock production – intensive or extensive – practised by the farm (9).

The waiting period is the period after the administration of a treatment, during which any food produced by the treated animal must not be marketed. It is determined on the basis of experimental studies conducted on target animals that are representative of the conditions of use but are in good health. The defined waiting period takes into account the pharmacokinetic variability between individual animals in the processes of absorption, distribution, metabolism and excretion of residues (active ingredients and metabolites). These processes depend on the physiological condition of the animal and the genetic traits influencing metabolism or excretion. The majority of these studies are carried out on breeds representative of large-scale production in developed countries and do not take into consideration the distinctive characteristics of African animal species, which may not only differ in terms of their genetic heritage (including acetylation rates) but whose physiology may be more suited to local climatic conditions (water consumption, volume of distribution and renal clearance). As these differences influence residue kinetics, an adjustment of the waiting period may be required when medicinal products are administered to local breeds. At this stage of development in veterinary drugs, such variations are not taken into account.

### **Control plans for antimicrobial residues in meat, offal and eggs**

In Europe, the prevalence of contamination by residues from medicinal products in foods of animal origin is less than 1% (43). In Africa, recent studies on the presence of antimicrobial residues in foods of animal origin are very limited. For example, a study on antimicrobial residues in chicken meat and offal in Dakar (Senegal) detected residues of prohibited substances such as nitrofurans and chloramphenicol in different matrices (44). In Ghana, the prevalence of antimicrobial residues is 30.8% for beef, 29.3% for kid goat meat, 28.6% for pork, 24% for lamb and 6.8% for eggs (9). In Nigeria, the

prevalence of antimicrobial residues is 0.1% to 1% for eggs (7, 45), 23.6% for laying hens, 4.8% for local chicken breeds and 21.8% for chicken faeces (45). Higher levels of 33.1% have been reported in Nigeria for chicken meat (45); 52% in gizzards and 81% in chicken livers in Senegal (44), as well as in Kenya (46) and Tanzania (47).

### **Control plans for antimicrobial residues in milk**

In the EU, processors frequently conduct controls for antimicrobial residues and there are systematic checks of bulk tankers to screen for the presence of inhibitors (48).

The absence of inhibitors is a quality criterion that increases the price that a farmer receives for milk. This is undoubtedly the reason why rates of non-compliant residues in milk are very low in the EU.

Very few studies have been devoted to evaluating antimicrobial residues in raw milk in African countries, with the exception of those in North Africa, because milk is not a staple food in these countries (9).

In Morocco, inhibitory substances were detected in raw milk, pasteurised milk, yoghurt, and the milk curd known as *raïbi* in the regions of Rabat and Kenitra (49). The authors of this study suggest that 42.87% of raw milk, 6.65% of pasteurised milk and 3.33% of *raïbi* may be contaminated by antimicrobial residues.

In Algeria, 89.09% of milk from farms in Wilayas, Blida, Algiers, Tipaza and Médéa tested positive for residues of tetracyclines and 65.46% for residues of beta-lactamines (50). Moreover, around 29% of milk samples taken in western Algeria contained antimicrobial residues (51). In the Algiers region, 9.87% of raw milk samples were found to be contaminated with residues: 97.33% of samples tested positive for penicillins and/or tetracyclines and 2.67% for macrolides and/or aminoglycosides (52).

In Mali, the prevalence of antimicrobial residues in samples of raw cows' milk was found to range from 6% to 16% (53), compared with 24.7% in Côte d'Ivoire (54).

## **Conclusion**

This review highlights a range of shortcomings in Africa with regard to antimicrobial residues. It also reveals a high prevalence of various antimicrobial residues in animal matrices. This points to a misuse of antimicrobials in livestock production, increasing the risk of selection of antimicrobial-resistant bacteria, which could cause serious infection in humans.

Antimicrobial residues in foods of animal origin are worrying because of the toxicological risk to consumers and the risk of non-compliance with the regulatory requirements for trade. In response to these concerns, it is essential to establish and continue to advance a national, sub-regional and regional legal framework in Africa. The control and surveillance of antimicrobials and their residues in foods of animal origin are key to ensuring the safety of animal-derived foodstuffs and to protecting consumers. However, to implement such controls, it is first necessary to update the legislation and draw up regulations modelled on those of the EU. A lack of surveillance programmes results in a lack of the scientific data required to inform political decision-makers, communicate with veterinarians and livestock producers, and support sustainable development policies. Study programmes must be set up to document all these aspects with a view to developing regulatory mechanisms and vocational training to meet the objectives of food security, food safety and the sustainable development of agrifood production in developing countries – both in Africa and elsewhere in the world.

## **References**

1. Moretain J.P. (2005). – Les résidus d’antibiotiques dans les aliments. Laboratoire d’études et de recherches sur les médicaments vétérinaires et les désinfectants, Agence Française de Sécurité Sanitaire des Aliments (AFSSA), Fougères, France, 18 pp.
2. Tatsadjieu Ngoume L., Tanedjieu K.S. & Mbofung C.M.F. (2009). – Impact de l’utilisation des antibiotiques sur la sensibilité des

bactéries pathogènes de poules dans la ville de Ngaoundéré. *Cameroun J. experim. Biol.*, **5** (2), 52–61.

3. Sanders P. (2005). – L'antibiorésistance en médecine vétérinaire : enjeux de santé publique et de santé animale. *Bull. Acad. vét. Fr.*, **158** (2), 137–142.

4. Sanders P., Bousquet-Melou A., Chauvin C. & Toutain P.L. (2011). – Utilisation des antibiotiques en élevages et enjeux de santé publique. *INRA Prod. anim.*, **24** (2), 199–204.

5. Baquero F. & Garau J. (2010). – Prudent use of antimicrobial agents: revisiting concepts and estimating perspectives in a global world. *Enferm. infecc. Microbiol. clín.*, **28**, 487–488.

6. Wassenaar T.M. (2005). – The use of antimicrobial agents in veterinary medicine and implications for human health. *Crit. Rev. Microbiol.*, **31**, 155–169.

7. Fagbamila I., Kabir J., Abdu P., Omeiza G., Ankeli P., Ngulukun S., Muhammad M. & Umoh J. (2010). – Antimicrobial screening of commercial eggs and determination of tetracycline residue using two microbiological methods. *Int. J. Poult. Sci.*, **9** (10), 959–962.

8. Hsieh M.K., Shyu C.L., Liao J.W., Franje C.A., Huang Y.J., Chang S.K., Shih P.Y. & Chou C.C. (2011). – Correlation analysis of heat stability of veterinary antibiotics by structural degradation, changes in antimicrobial activity and genotoxicity. *Vet. Med.*, **56** (6), 274–285.

9. Donkor E.S., Newman M.J., Tay S.C.K., Dayie N.T.K.D., Bannerman E. & Olu-Taiwo M. (2011). – Investigation into the risk of exposure to antibiotic residues contaminating meat and egg in Ghana. *Food Control*, **22**, 869–873.

10. Tarawali S., Herrero M., Descheemaeker K., Grings E. & Blümmel M. (2011). – Pathways for sustainable development of

mixed crop livestock systems: taking a livestock and pro-poor approach. *Livest. Sci.*, **139**, 11–21.

11. Messomo Ndjana F. (2006). – Étude de la distribution et de la qualité des médicaments vétérinaires au Cameroun. PhD thesis submitted to the École Inter-états des Sciences et Médecine Vétérinaires (EISMV), Dakar, Senegal, 114 pp.

12. Food and Agriculture Organization of the United Nations (FAO) (2007). – Food safety risk analysis. A guide for national food safety authorities. FAO Food and Nutrition Paper 87. FAO, Rome, 145 pp. Available at: <ftp://ftp.fao.org/docrep/fao/010/a0822f/a0822f.pdf> (accessed on 14 July 2012).

13. Lefeuvre C. (2003). – La gestion des risques sanitaires induits par le médicament vétérinaire : place de la traçabilité. Mémoire de l'École Nationale de Santé Publique, France, 53 pp.

14. European Food Safety Authority (EFSA) (2012). – The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2010. *EFSA J.*, **10** (3), 233 pp.

15. West African Economic and Monetary Union (UEMOA) (2007). – Règlement n° 0072007/CM/UEMOA relatif à la sécurité sanitaire des végétaux, des animaux et des aliments dans l'UEMOA. Available at: [www.uemoa.int/Documents/Actes/Reglement\\_07\\_relatif\\_à\\_la\\_securite\\_sanitaire.pdf](http://www.uemoa.int/Documents/Actes/Reglement_07_relatif_à_la_securite_sanitaire.pdf) (accessed on 25 May 2012).

16. Mensah G.A. & Houssou P.A. (2010). – Atelier technique sur l'analyse des risques sanitaires des aliments. *In* Rapport final de l'atelier. Cotonou, Benin, 24 pp.

17. Mensah G.A. (2011). – Atelier technique sur l'analyse des risques sanitaires des aliments. *In* Rapport final de l'atelier. Cotonou, Benin, 14 pp. Available at: [www.fao.org/fileadmin/user\\_upload/agns/pdf/Rapport\\_atelier\\_FAO\\_OMS\\_\\_INRAB\\_Cotonou\\_dec\\_2011.pdf](http://www.fao.org/fileadmin/user_upload/agns/pdf/Rapport_atelier_FAO_OMS__INRAB_Cotonou_dec_2011.pdf) (accessed on 14 July 2012).

18. Aning K.G., Donkor E.S., Omore A., Nurah G.K., Osafo E.L.K. & Staal S. (2007). – Risk of exposure to marketed milk with antimicrobial drug residues in Ghana. *Open Food Sci. J.*, **1**, 1–5.

19. Agence Française de Sécurité Sanitaire des Aliments (AFSSA) (2006). – Usages vétérinaires des antibiotiques, résistance bactérienne et conséquences pour la santé humaine. Rapport du Groupe de travail de l'AFSSA sur l'antibiorésistance. AFSSA, Maison-Alfort, 214 pp.

20. Cazeau G., Chazel M., Jarrige N., Sala C., Calavas D. & Gay E. (2010). – Utilisation des antibiotiques par les éleveurs en filière bovine en France. In 17<sup>e</sup> Journées rencontres recherche ruminants, 71–74. Available at: [www.journees3r.fr/spip.php?article2978](http://www.journees3r.fr/spip.php?article2978) (accessed on 17 January 2012).

21. Labro M.T. (2012). – Immunomodulatory effects of antimicrobial agents. Part I: antibacterial and antiviral agents. *Expert Rev. anti-infect. Ther.*, **10** (3), 319–340.

22. European Commission (EC) (2010). – Commission Regulation (EU) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin. *Off. J. Eur. Union*, **L 15**, 1–72. Available at: [http://ec.europa.eu/health/files/eudralex/vol-5/reg\\_2010\\_37/reg\\_2010\\_37\\_en.pdf](http://ec.europa.eu/health/files/eudralex/vol-5/reg_2010_37/reg_2010_37_en.pdf) (accessed on 13 August 2014).

23. Teko-Agbo A., Biauou F.C., Akoda K., Faure P. & Abiola F.A. (2003). – Contrefaçons et malfaçons de trypanocides à base de diminazène et d'anthelminthiques contenant de l'albendazole au Bénin et au Togo. *Rev. afr. Santé Prod. Anim.*, **1** (1), 39–47.

24. Abiola F.A. (2001). – Qualité des anthelminthiques et des trypanocides au Cameroun (étude préliminaire par sondage limité). In Rapport d'expertise, École Inter-états des Sciences et Médecine Vétérinaires (EISMV), Dakar, Senegal, 12 pp.

25. Abiola F.A. (2002). – Qualité des anthelminthiques et des trypanocides en Mauritanie (étude préliminaire par sondage limité). *In* Rapport d'expertise, École Inter-états des Sciences et Médecine Vétérinaires (EISMV), Dakar, Senegal. 13 pp.

26. Abiola F.A. (2005). – Qualité des médicaments vétérinaires prélevés au Tchad. *In* Rapport d'expertise, École Inter-états des Sciences et Médecine Vétérinaires (EISMV), Dakar, Senegal, 13 pp.

27. Biagui C. (2002). – Utilisation des médicaments vétérinaires en élevage avicole dans la région de Dakar ; qualité de la viande à travers la recherche de résidus de substances à activité antimicrobienne (antibiotiques). PhD thesis in veterinary medicine submitted to the École Inter-états des Sciences et Médecine Vétérinaires (EISMV), Cheick Anta Diop University, Dakar, Senegal, 153 pp.

28. Anonrin S. (2004). – Enregistrement des médicaments vétérinaires: une commission technique installée. *Le Matinal*, 18 October 2004. Available at: [nt7.h2com/Imo\\_article.cfm?article\\_num=18253](http://nt7.h2com/Imo_article.cfm?article_num=18253) (accessed on 18 October 2004).

29. European Commission (1981). – Council Directive 81/852/EEC of 28 September 1981 on the approximation of the laws of the Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of the testing of veterinary medicinal products. *Off. J. Eur. Communities*, **L 317**, 16–28.

30. Codex Alimentarius Commission (CAC) (2011). – Maximum residue limits for veterinary drugs in food. CAC, Rome, 36 pp.

31. André F. (2003). – Interpretation of EC testing requirements as described in Directive 96/23. Communication. Pretoria, South Africa, 93 slides.

32. European Commission (2002). – Commission Decision of 12 August 2002 implementing Council Directive 96/23/EC concerning the performance of analytical methods and the interpretation of results. *Off. J. Eur. Communities*, **L 221**, 8–36.

33. Pikkemaat M.G., Rapallini M.L.B.A., Oostra-Van Dijk S. & Elferink J.W.A. (2009). – Comparison of three microbial screening methods for antibiotics using routine monitoring samples. *Analyt. chim. acta*, **637**, 298–304.

34. Ferguson J.P., Baxter G.A., McEvoy J.D.G., Stead S., Rawlings E. & Sharman M. (2002). – Detection of streptomycin and dihydrostreptomycin residues in milk, honey and meat samples using an optical biosensor. *Analyst*, **127**, 951–956.

35. Gaudin V., Cadieu N. & Sanders P. (2005). – Results of a European proficiency test for the detection of streptomycin/dihydrostreptomycin, gentamicin and neomycin in milk by ELISA and biosensor methods. *Analyt. chim. acta*, **529**, 273–283.

36. Stolker A.A.M. & Brinkman U.A.T. (2005). – Analytical strategies for residue analysis of veterinary drugs and growth-promoting agents in food-producing animals – a review. *J. Chromatogr., A*, **1067** (1–2), 15–53.

37. Msagati T.A.M. & Nindi M.M. (2007). – Determination of  $\beta$ -lactam residues in foodstuffs of animal origin using supported liquid membrane extraction and liquid chromatography mass spectrometry. *Food Chem.*, **100**, 836–844.

38. McGlinchey T.A., Rafter P.A., Regan F. & McMahon G.P. (2008). – A review of analytical methods for the determination of aminoglycoside and macrolide residues in food matrices. *Analyt. chim. acta*, **624**, 1–15.

39. Cristofani E., Antonini C., Tovo G., Fioroni L., Piersanti A. & Galarini R. (2009). – A confirmatory method for the determination of tetracyclines in muscle using high-performance

liquid chromatography with diode-array detection. *Analyt. chim. acta*, **637**, 1–2.

40. Mamani M.C.V., Reyes F.G.R. & Rath S. (2009). – Multiresidue determination of tetracyclines, sulphonamides and chloramphenicol in bovine milk using HPLC-DAD. *Food Chem.*, **117**, 545–552.

41. Spisso B.F., De Araujo Jr M.A.G., Monteiro M.A., Lima A.M.B., Pereira M.U., Luiz R.A. & da Nóbrega A.W. (2009). – A liquid chromatography-tandem mass spectrometry confirmatory assay for the simultaneous determination of several tetracyclines in milk considering keto-enol tautomerism and epimerization phenomena. *Analyt. chim. acta*, **656** (1–2), 72–84. doi:10.1016/j.aca.2009.10.012.

42. Form G. (2003). – Les résidus inhibiteurs dans le lait. Évolution des méthodes de détection. Facteurs de risque en région Rhône-Alpes. PhD thesis in veterinary medicine submitted to Université Claude Bernard-Lyon 1, 102 pp.

43. European Commission (EC) (2005). – Report on the results of residue monitoring in food of animal origin in the Member States. EC, Brussels.

44. Abiola F.A., Diop M.M., Teko-Agbo A., Delepine B., Biaou F.C., Roudaut B., Gaudin V. & Sanders P. (2005). – Résidus d'antibactériens dans le foie et le gésier de poulets de chair dans les régions de Dakar et de Thiès (Sénégal). *Rev. Méd. vét.*, **156** (5), 264–268.

45. Kabir J., Umoh V.J., Audu-Okoh E., Umoh J.U. & Kwaga J.K.P. (2004). – Veterinary drug use in poultry farms and determination of antimicrobial drug residues in commercial eggs and slaughtered chicken in Kaduna State, Nigeria. *Food Control*, **15**, 99–105.

46. Kang'ethe E.K., Aboge G.O., Arimi S.M., Kanja L.W., Omore A.O. & McDermott J.J. (2005). – Investigation of risk of

consuming marketed milk with antimicrobial residues in Kenya. *Food Control*, **16**, 349–355.

47. Kurwijila L.R., Omore A., Staal S. & Mdoe N.S.Y. (2006). – Investigation of the risk of exposure to antimicrobial residues present in marketed milk in Tanzania. *J. Food Protec.*, **69** (10), 2487–2492.

48. European Commission (EC) (2010). – Commission staff working document on the implementation of national residue monitoring plans in the Member States in 2009 (Council Directive 96/23/EC) [final], 323 pp. Available at: [http://ec.europa.eu/food/food/chemicalsafety/residues/workdoc\\_2009\\_en.pdf](http://ec.europa.eu/food/food/chemicalsafety/residues/workdoc_2009_en.pdf) (accessed on 13 August 2014).

49. Zinedine A., Faid M. & Benlemlih M. (2007). – Détection des résidus d'antibiotiques dans le lait et les produits laitiers par méthode microbiologique. *Rev. Microbiol. indust. sanit. environ.*, **1**, 1–9.

50. Tarzaali D., Dechicha A., Gharbi S., Bouaissa M.K., Yamnaine N. & Guetarni D. (2008). – Recherche des résidus des tétracyclines et des bêta-lactamines dans le lait cru par le MRL Test (ROSA TEST) à Blida, Algérie. *In* 6<sup>e</sup> Journées scientifiques vétérinaires sur le médicament vétérinaire : nouvelles approches thérapeutiques et impact sur la santé publique, École Nationale Vétérinaire, Algeria, 23–24.

51. Aggad H., Mahouz F., Ahmed Ammar Y. & Kihal M. (2009). – Évaluation de la qualité hygiénique du lait dans l'Ouest algérien. *Rev. Méd. vét.*, **160** (12), 590–595.

52. Ben-Mahdi M.H. & Ouslimani S. (2009). – Mise en évidence de résidus d'antibiotiques dans le lait de vache produit dans l'Algérois. *Eur. J. sci. Res.*, **36** (3), 357–362.

53. Bonfoh B., Dem S., Keita O., Delorenzi S., Traore H., Simbe C.F., Alfaroukh I.O., Farah Z., Nicolet J. & Zinsstag J. (2003). – Assessment of antibiotic residues by microbial inhibitor tests

in fresh cow milk sold in Bamako (Mali). *Milchwissenschaft*, **58** (5–6), 304–307.

54. Kouame-Sina S.M., Bassa A., Dadie A., Makita K., Grace D., Dje M. & Bonfoh B. (2010). – Analyse des risques microbiens du lait cru local à Abidjan (Côte-d’Ivoire). *Rev. afr. Santé Prod. Anim.*, **8**, 36–42.

---

**Table I**  
**Main classes and molecules of antibiotics and antimicrobials authorised in the European Union (22)**

Class	Molecules	Antimicrobial action	Spectrum of activity
Sulfamides	All substances belonging to the group of sulfonamides*	Inhibit the synthesis of folates by the action of competitive inhibitors of dihydropteroate synthase	Gram-positive cocci
Quinolones	Oxolinic acid, difloxacin, sarafloxacin, danofloxacin, enrofloxacin*, flumequine*, marbofloxacin	Inhibit the gyrase of bacterial DNA or the topoisomerase IV, thereby inhibiting DNA replication and transcription	Broad-spectrum on <i>Mycobacterium tuberculosis</i> (fluoroquinolones, in combination with other antimicrobials)
Beta-lactamines	Amoxicillin*, ampicillin, benzylpenicillin*, cefalexin, cefacetrile, cefalonium, cephapirin, cefaperadone, cefquinome, ceftiofur, cefazolin, cloxacillin, cefoperazone, penethamate, dicloxacillin, nafcillin, oxacillin	Beta-lactamines disrupt the synthesis of the peptidoglycan layer on the cell walls of bacteria by binding to the proteins contributing to synthesis	Gram-positive cocci Gram-positive and Gram-negative bacteria, <i>Treponema pallidum</i> , <i>Borrelia</i>
Tetracyclines	Chlortetracycline*, doxycycline*, oxytetracycline**, tetracycline*	Bind with ribosomal 30S sub-units, inhibiting binding of aminoacyl-tRNA to the mRNA-ribosome complex	<i>Treponema pallidum</i> , <i>Chlamydia</i> , <i>Borrelia</i> , <i>Rickettsia</i> , <i>Plasmodium falciparum</i>
Aminoglycosides	Dihydrostreptomycin*, gentamicin, kanamycin, neomycin*, streptomycin, paromomycin, apramycin, spectinomycin	Bind with bacterial ribosome 30S sub-units (some bind with 50S sub-units), inhibiting the translocation of peptidyl-tRNA from the A site to the P site and causing erroneous reading of the mRNA	Gram-positive and Gram-negative bacteria (including <i>Pseudomonas aeruginosa</i> ) <i>Mycobacterium tuberculosis</i>
Phenolics	Thiamphenicol, florfenicol	Bind reversibly with bacterial ribosome 50S sub-units, preventing the formation of peptide bonds	<i>Neisseria meningitidis</i> , <i>Salmonella Typhi</i>
Macrolides	Erythromycin*, spiramycin*, tylosin*, tilmicosin, gamithromycin, tulathromycin, tylvalosin, tildipirosin	Bind reversibly with bacterial ribosome 50S sub-units, inhibiting the translocation of peptidyl-tRNA	Gram-positive cocci, <i>Treponema pallidum</i> , intracellular pathogens, <i>Mycoplasma</i> , <i>Plasmodium falciparum</i>
Lincosamides	Lincomycin, pirlimycin	Bind with ribosomal 50S sub-units, inhibiting transpeptidation/translocation	Gram-positive cocci, anaerobic (clindamycin) <i>Plasmodium falciparum</i> (clindamycin)
Polypeptides	Bacitracin, colistin, tyrothricin	React strongly with membrane phospholipids and disrupt the functioning and permeability of these membranes	Gram-positive and Gram-negative bacteria <i>Bacillus polymyxa</i> , <i>Bacillus subtilis</i>

---

Orthosomycins	Avilamycin		Gram-positive bacteria
Rifamycins	Rifamycin SV, rifaximin rifampicin	Block the synthesis of messenger RNA	Gram-positive and Gram-negative cocci, Gram-positive bacilli Broad-spectrum
Ionophores	Salinomycin, monensin		Gram-positive bacteria, coccidiostatic
Novobiocin	Novobiocin	Inhibit DNA replication	Gram-positive and Gram-negative cocci, Gram-positive bacilli, <i>Haemophilus</i> , <i>Pasteurella</i>
Pleuromutilins	Tiamulin, valnemulin	Inhibit protein synthesis in ribosomal 50S sub-units	Broad-spectrum

---

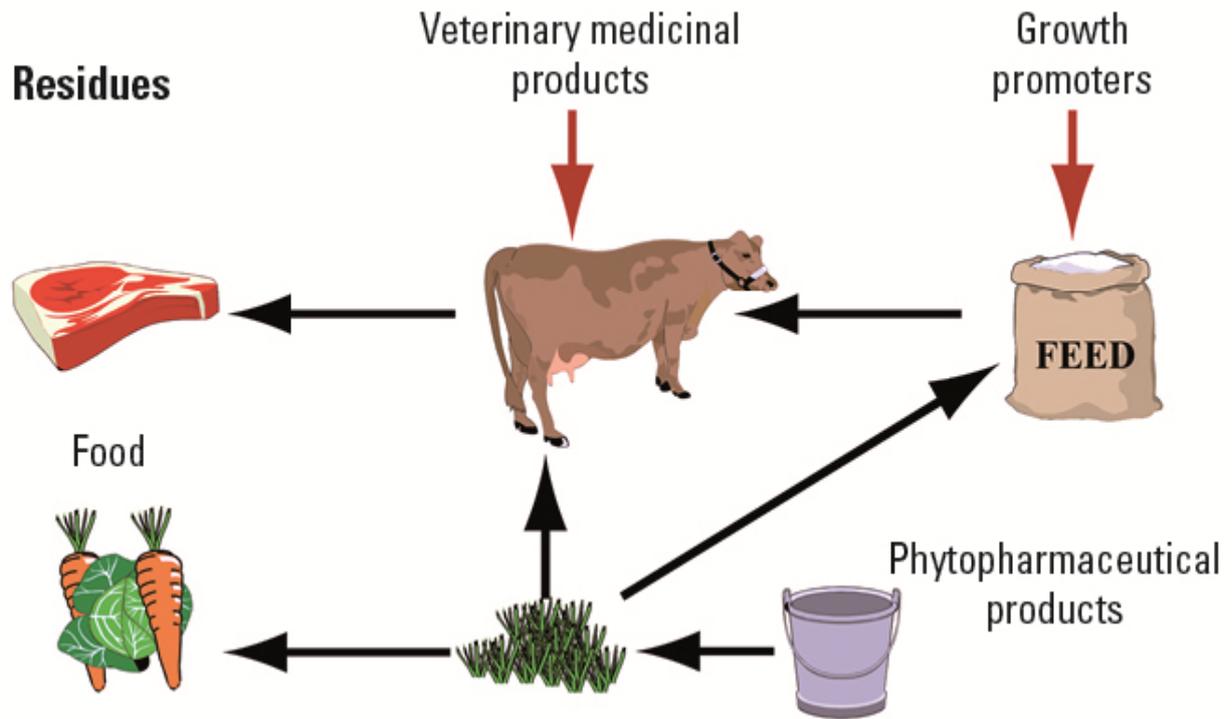
\* Molecule approved in Benin

\*\* Molecule approved in the West African Economic and Monetary Union and in Benin

**Table II**  
**Main classes of antimicrobials and potential risks (22)**

Class	Health risks
Sulfamides	Allergies (with skin rashes), Sweet's syndrome, DRESS syndrome, leukopaenia
Quinolones	Immediate hypersensitivity reactions (urticaria, angioedema, anaphylaxis), exanthema, Sweet's syndrome
Beta-lactamines	Immediate reactions: urticaria, angioedema, rhinitis, bronchospasm and anaphylaxis, haemolytic anaemia, neutropaenia, eosinophilia. Skin rashes, Stevens-Johnson syndrome, Lyell's syndrome
Tetracyclines	Drug hypersensitivity syndrome, drug-induced lupus erythematosus such as a rash, anaphylaxis, DRESS syndrome, Sweet's syndrome
Aminoglycosides	Allergic contact dermatitis
Phenicol	Rare bone marrow suppression: aplastic anaemia
Macrolides	Rare
Lincosamides	Neuromuscular blockade with post-anaesthetic paralysis, cardiac depression after too rapid IV injection, allergies and moderate hepatic degeneration

DRESS syndrome: drug reaction (or rash) with eosinophilia and systemic symptoms syndrome



**Fig. 1**  
**Formation of residues in food**  
*Source: André (2003) (31)*