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of the International Dairy Federation

**Identification and
assessment of emerging
issues associated with
chemical contaminants
in dairy products**



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Identification and assessment of emerging issues associated with chemical contaminants in dairy products

FOREWORD

This IDF Bulletin comprises the paper “Identification and assessment of emerging issues associated with chemical contaminants in dairy products” presented at the Food Safety Conference organized during the IDF World Dairy Summit, Cape Town, in October 2012.

The IDF World Dairy Summit 2012 brought together many stakeholders of the dairy chain and offered a unique platform for companies, academia and dairy leaders to share their knowledge and experience. It also provided an opportunity for people involved in the field to engage in a frank and open discussion about innovative research, the progress achieved and lessons learnt.

The next IDF World Dairy Summit will take place in 2013 in Yokohama, Japan. On behalf of IDF, I look forward to welcoming you all there.

Nico van Belzen, PhD
IDF Director General
International Dairy Federation
Brussels, July 2013

Identification and assessment of emerging issues associated with chemical contaminants in dairy products

L. D. Feijó*, M. S. Fleury, A. J. Portz, R. L. Castelo Branco, R. S. Rocha and A. M. S. Silva
Coordination of Residues and Contaminants of the Secretariat of Animal and Plant Health and Inspection from the Ministry of Agriculture, Livestock and Supply (MAPA). Esplanada dos Ministérios, Annex B, Block D, Room 448, CEP: 70043–900, Brasília/DF, Brazil
 *Communicating author: leandro.feijo@agricultura.gov.br

ABSTRACT

Food safety has gained great importance in the international scenario, primarily due to the recognition by the public of the risks posed from unsafe food. In this context, studies are being developed to provide safe food for the population. Thus, the Brazilian Ministry of Agriculture, Livestock and Supply monitors residues of antibiotics, antiparasitics and other substances in animal products in order to identify whether the levels of such substances are at safe concentrations for human consumption.

Keywords: Antimicrobial, Antiparasitic, Contaminant, Dairy, Food safety, Milk, Risk analysis

1. INTRODUCTION

Nowadays, food safety is more and more the focus of national and international public health policies and the food trade. In this context, the presence of residues, mostly from antibiotics, antiparasitics and contaminants, in food of animal origin is a subject of great importance.

The monitoring of residues in milk has a major importance in this framework, given that milk is usually consumed daily and especially as the main sector of the population that consumes this product and its derivatives is composed of children and the elderly and it is these groups that are more susceptible to adverse health effects related to ingestion of contaminated products [1, 2].

The dairy industry is extremely important in the Brazilian economy, involving the entire production chain from farm to the final consumer, and stands out as one of the four main sectors of the Brazilian food industry. However, crucial points in this sector are the non-observance of Good Agricultural Practices (GAP), misuse of veterinary products and non-compliance with the withholding period (WHP). These and other practices may result in the presence of residues with toxic effects or the development of bacterial and parasitic resistance to antimicrobial and antiparasitic products.

With the objective of risk mitigation, the monitoring and risk analysis of such residues should take into account the Brazilian dairy production system (use of collective cooling tanks, the “dilution effect”, herd and individual treatment of cattle, etc.) [3, 4].

2. RESIDUES AND CONTAMINANTS

The presence of residues and contaminants in food is considered a hazard to human health; however, studies are needed to determine the real risk involved in the consumption of those foods [1, 3, 5].

Residues and contaminants are chemical substances found in foods consumed daily and present a potential toxicological risk. They include residues from substances used in livestock production and contaminants transferred from the environment to the production chain [6].

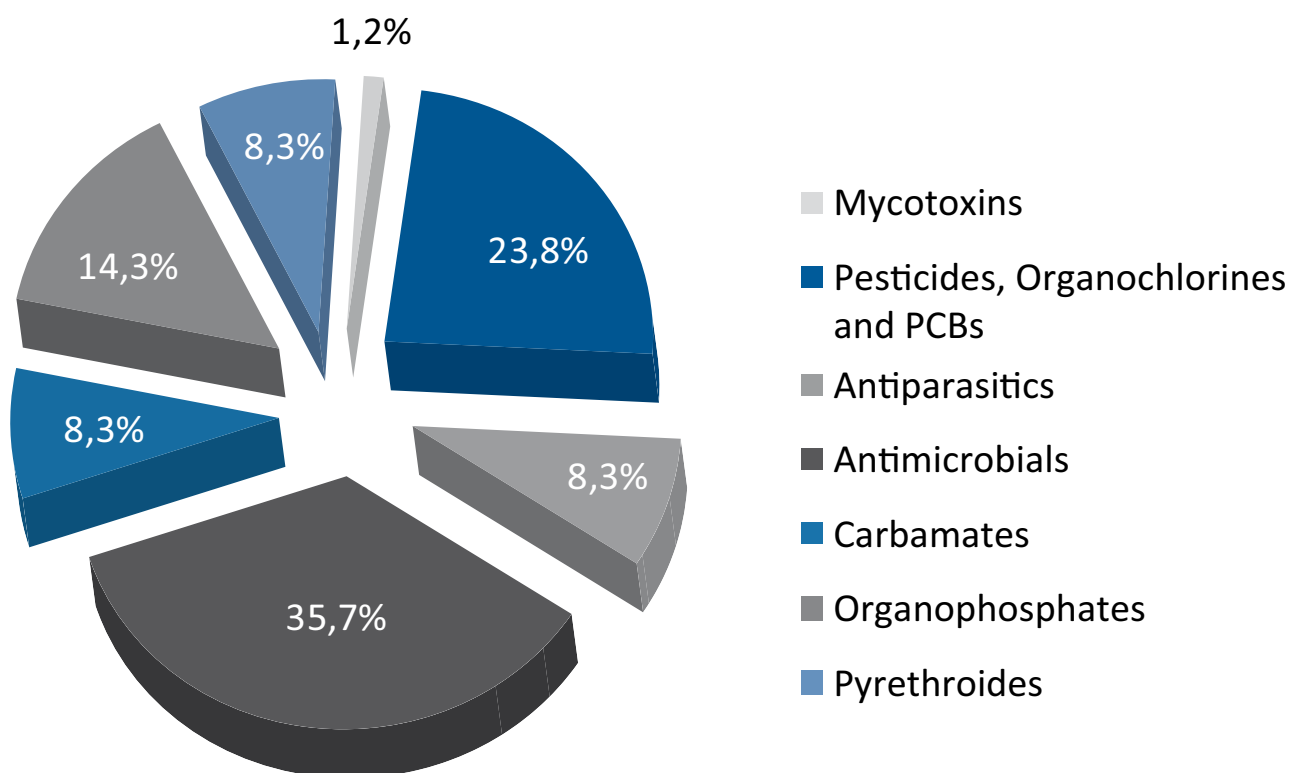
Thus, it becomes necessary and indispensable to monitor residues in milk available for consumption. In Brazil, official monitoring was established by the Ministry of Agriculture, Livestock and Supply (MAPA), through the National Plan for Control of Residues and Contaminants in Animal Products (PNCRC) [7].

2.1. NATIONAL PLAN FOR CONTROL OF RESIDUES AND CONTAMINANTS

The PNCRC is an official tool from MAPA for risk management, established in 1978 and regulated in 1999 by the Normative Instruction no. 42 of

December 20, which enables the monitoring for detection and/or quantification of residues from veterinary products and contaminants in products of animal origin. This Plan is aligned to the recommendations of several international agencies for food safety and with the principles of risk analysis recommended by the Codex Alimentarius Committee/FAO/WHO. The analytical scope of the program is published annually and describes the analytes to be monitored, as well as their respective reference limits and the number of samples to be analyzed.

Figure 1: Groups of analytes monitored in milk – PNCRC 2012 [8]



These samples are collected in slaughterhouses and food processing establishments under the aegis of the Federal Inspection Service (SIF), randomly or biased, depending on the scope of the subprogram to which it belongs, i.e., monitoring, investigation or exploratory subprograms. There is also a subprogram for monitoring of imported products, which enables

products of animal origin imported into Brazil to be analyzed for the presence of residues and contaminants [7].

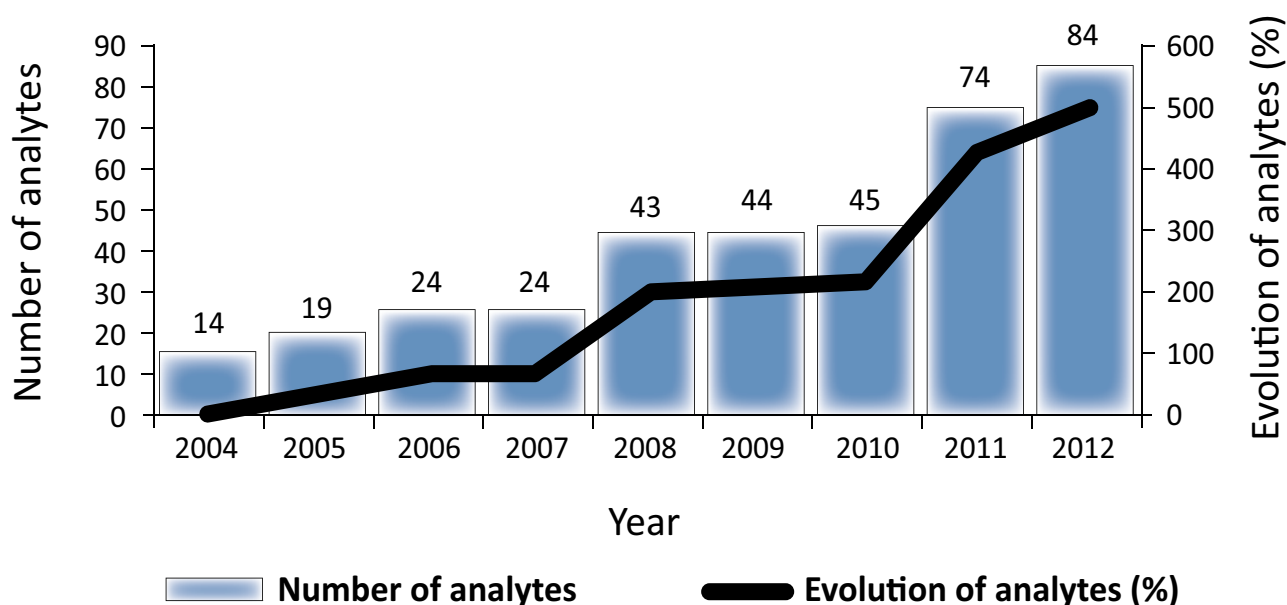
Laboratory analyses are carried out in laboratories of the National Official Agricultural and Livestock Laboratories Network (LANAGRO), which is composed of public and private laboratories, all

accredited according to the ISO 17025 standard. The analysis of these samples are performed by means of the detection and/or quantification of residues of the substances defined in the scope, and its results are compared to the maximum residue limits (MRLs), i.e., the maximum amount of residues officially accepted in certain matrices. If the results found in the analysis exceeds the MRL set for the analyte, a non-compliance is

detected, which may indicate non-observance of GAP [7].

The milk matrix became part of PNCRC in 2004, when 14 analytes were included in the scope. Currently, they are part of the scope of 84 analytes, representing a 500% increase in scope [8].

Figure 2: Evolution of the monitored analytical scope of PNCRC [8]



2.2. ANTIBIOTICS

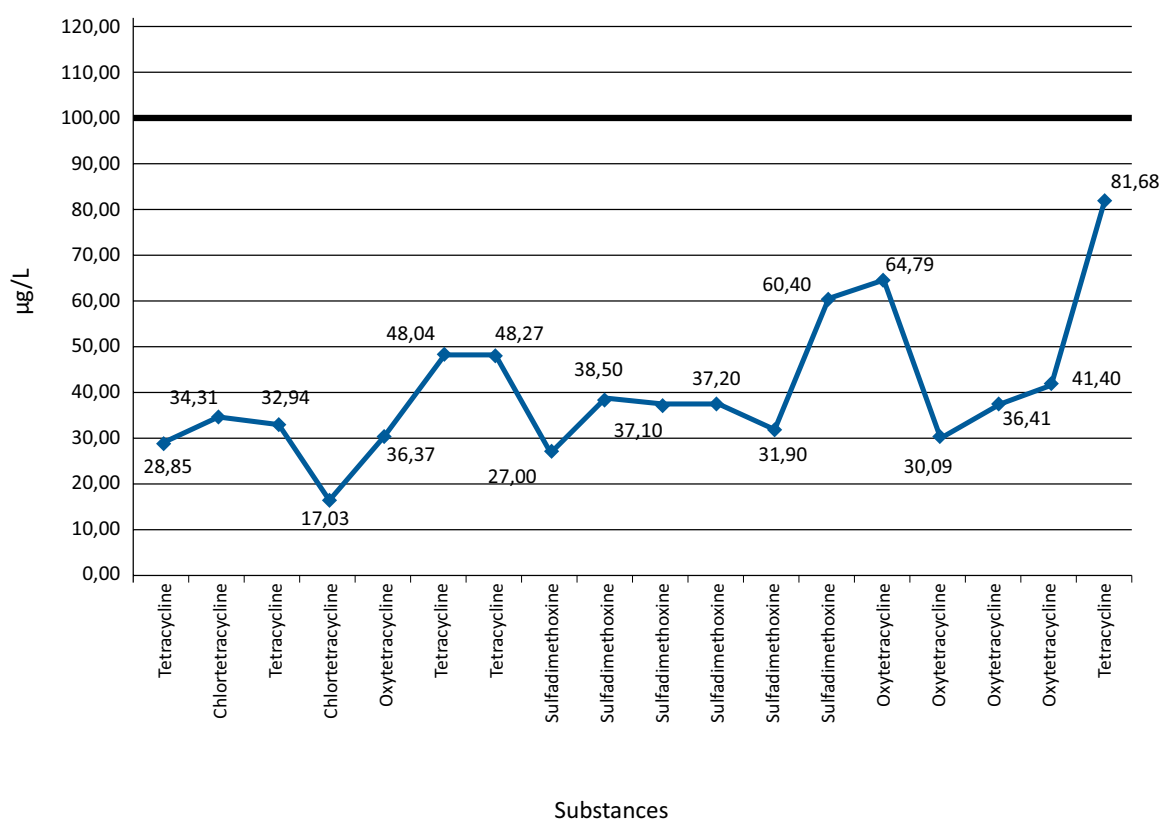
The discovery of penicillin in 1940, the continuing development of antibiotics between 1920 and 1970, and the widespread use of these over the years have resulted in the false sense of security that diseases caused by bacteria can no longer cause harm to human or animal health. However, the widespread use of new drugs has generated the selection of strains resistant to therapeutic doses of antimicrobials [5].

The presence of antimicrobial residues in food of animal origin is one of the factors responsible for the development of resistant strains. These resistant strains are the result of therapeutic, prophylactic and “growth promoter” use of antimicrobials when use is indiscriminate and there is no respect for the WHP [1, 3]. The presence of such residues may provoke effects

on human health (hypersensitivity, anaphylactic shock, teratogenicity and imbalance of the microbiota in the human body) as well as losses to the dairy industry (interference in the production of derivatives such as yogurt and cheese) [3].

Currently, antimicrobial resistance has become a major concern for food safety and public health worldwide [9]. Creation of the European Antimicrobial Resistance Surveillance System (EARSS) is an example of this concern and comprises various laboratories and studies of several pathogens. EARSS has shown the consequences of the indiscriminate use of antibiotics, demonstrating that resistance rates have grown considerably in recent decades throughout Europe, especially when dealing with Gram-negative bacilli. However, the magnitude of this growth and its consequences are not yet known [9].

Figure 3: Detection of residues (below the MRLs) from January 2008 to May 2012 –PNCRC/Milk/2012 [4]



2.3. ANTIPARASITICS

The struggle against ecto- and endoparasites is an issue that has worried not only researchers, but also producers around the world. There is therefore a search for antiparasitic drugs with greater efficacy, lower toxicity to living beings and the environment and with greater “residual power”, i.e. they remain acting for a longer time against the target parasites [10]. Along with this, the resistance of parasites, both internal and external, to antiparasitics is increasingly becoming a major concern for livestock producers [11].

In this scenario, there is greater demand from industry and society to obtain milk with residue levels of antiparasitic drugs in accordance with worldwide acceptable standards. The aim is for food safety and, when the subject involves food quality, the presence of consumer demands for a stricter legislation is increasingly more evident [10].

The macrocyclic lactones have, for years, been the most widely used antiparasitic for animal treatment, including food-producing animals [12].

Existing since the 1980s, these drugs produced a great revolution in the world market for antiparasitic drugs because of their activity against ectoparasites and control over endoparasites [10, 12, 13].

The concerns related to the presence of residues of antiparasitics, including macrocyclic lactones in milk, are magnified when dealing with products that contain unapproved substances in their composition. Concerns are due mainly to the fact that these chemicals can be excreted in milk after treatment and, in the case of macrocyclic lactones, up to 5% residual concentration can be found [12].

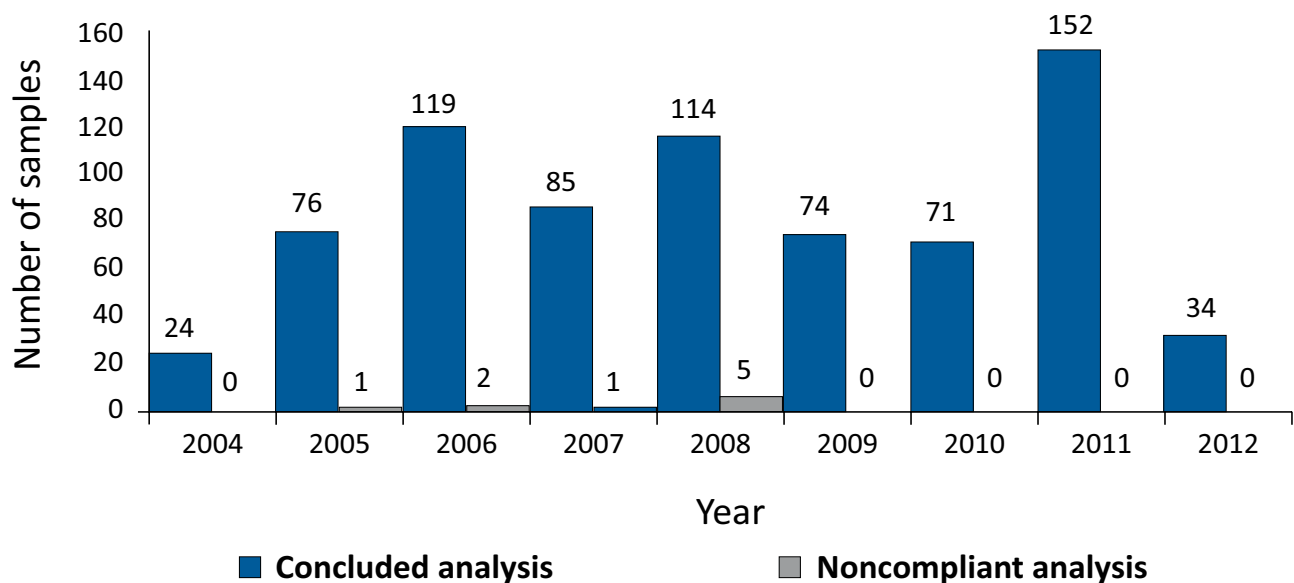
Generally, when dairy cows are in lactation period, ivermectin and moxidectin should not be used unless the WHP is observed. However, based on the knowledge that moxidectin has less toxicity compared with ivermectin, in some jurisdictions it is registered as “pour-on” for use in dairy cows, with milk WHP equal to zero [14].

In the European Union, ivermectin is not licensed for use in species during lactation. For this reason, studies have been conducted in

several species in order to measure the residue depletion rate after administration of ivermectin. Although ivermectin is not licensed for use in lactating species in the European Union, one macrocyclic lactone, eprinomectin, is licensed for this use. This is probably because of the peculiar pharmacokinetics of this substance, which is characterized by only 0.1% of the dose being excreted in milk after “pour-on” use in dairy cows. In this case, the WHP was set to null for milk [12].

Regarding the non-compliance warnings about these substances, in analyzes performed on several species in the USA from 1988 to 1990, benzimidazole residues, including albendazole, were not detected in a group of 6000 samples. From a total of 10,052 samples collected, residues of ivermectin were only found in 20 samples [15]. Moreover, in Brazil during the period 2004–2012, MAPA, with the PNCRC, analyzed samples of cow’s milk for residues of ivermectin and found only 9 samples out of 745 that were non-conforming [8].

Figure 4: Monitoring of ivermectin in milk – PNCRC [8]



2.4. MYCOTOXINS

Mycotoxins are produced from fungal colonization of food from animal origin or cereal, making them potentially hazardous because of their toxicity. Human exposure to these toxins and their effects have been widely studied, being an important issue for food safety [2, 16,].

Examples of mycotoxins that contribute a risk to human health include B1/M1 aflatoxin, A ochratoxin, deoxynivalenol, B1 fumonisin, zearalenone and T-2 toxin [16]. Aflatoxin is a secondary metabolite of the fungus *Aspergillus flavus* and its indirect source is milk and its products. What is known about this fungus is that when lactating animals consume contaminated food, they can ingest B1 aflatoxin (AFB1), which is biotransformed to a hydroxylated metabolite

called M1 aflatoxin (AFM1) [17]. This metabolite is secreted through milk and is considered harmful to human health because of its genotoxic, mutagenic and carcinogenic potential, being directly related to the occurrence of liver cancer [2, 16].

In this sense, milk is increasingly a more and more important disseminator of AFM1 in the human diet. Therefore, the possibility of the presence of AFM1 in milk and dairy products increasingly arouses attention and concern when dealing with food safety [2].

In Brazil, specifically in the city of São Paulo, in the period from September to November of 2006, 125 samples of milk from kindergartens and schools (65 samples of milk powder) and from supermarkets (60 samples; 10 of these being

milk powder, 10 pasteurized and 40 UHT) were analyzed. It was found that 119 (95.2%) were contaminated with AFM1, with detectable levels from 10 ng/L. Of these, 47 (94.0%) represented fluid milk and 72 (96.0%) represented milk powder. A total of 33 (26.4%) samples showed detectable high levels of 50 ng/kg [2].

The formation of aflatoxins in food is recurrent and difficult to avoid. Specific regulations to control AFB1 and monitoring programs for AFM1 in food by accurate analytical techniques must be implemented and carried out for the benefit of public health and aiming to mitigate risks [2]. There is evidence that mycotoxins will never be completely removed from the food chain, although it is believed that the level of exposure through milk can be controlled to levels below those recommended by the European Union [16].

2.5. DIOXINS

Dioxins do not occur naturally in the environment; they were intentionally produced primarily between the years 1930 and 1970 and have a wide range of applications, such as seals and electrical capacitors. Currently, contamination occurs through leakage or accidental and illegal discharge from thermal processes, mainly by air, but may also be dispersed by accidental combustion (domestic and industrial) [18]. However, in general, dioxins are detectable and persistent in most environments around the world [19]. The discovery of its toxicity was in 1957 due to the first dioxin crisis, and over one million broiler chickens died unexpectedly in the USA [20]. Studies showed that these substances have toxic effects (carcinogenic, reduction of thymus function, endocrine dysfunction, immunotoxicity, reproductive damage, teratogenicity), both in animals and in humans [18].

By having a very slow degradation period, most of the current exposure occurs due to old contamination. Therefore, the livestock is contaminated mainly by food, coming into contact with the dioxins in feed and pasture or contaminated supplements, and also by air. Thus, the amount of dioxin present in animal fat is directly related to environmental contamination (environmental reservoirs or tanks) or contamination of feed. Because of its

lipophilic characteristics and affinity for aromatic hydrocarbons, this substance tends to accumulate in adipose tissues and fatty substances, contaminating the animals while they go through the food chain [18, 19].

During feeding, dairy cows can be contaminated and excrete these toxins into the milk. Along with their derivatives, these excreted dioxins are responsible for 32–43% of human exposure to dioxin, and 95% of dioxins in the human body comes from food. The percentage of this contaminant in milk depends on the amount present in the animal feed as well as on environmental contamination [8].

In recent years, the analysis of dioxins contaminating milk has become an important factor, the established allowable limits for dioxins in food becoming increasingly more restricted and specific [20, 21]. The Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the Scientific Committee on Food (SCF) of the European Union have established tolerable intake levels and compared them with the estimated daily intake. They concluded that a considerable proportion of the population may exceed tolerable intake of dioxins [18].

3. RISK ANALYSIS

Risk analysis consists of a set of measures previously defined as “activities of preliminary risk management”, which allows the manager to adopt the most appropriate action in relation to the risk assessed. This action may be to establish a policy of risk assessment, which will use data provided through the activities of risk management. Besides the evaluation, it is necessary, within the process of risk analysis, to identify, select and implement risk management actions, by the managers, in order to mitigate the risk to human health. For the process to be efficient, good communication between risk assessors and managers, and between these and other stakeholders is needed [1].

Agribusiness makes up the largest Brazilian economic activity and still holds high uncertainty and variability inherent to the biological, chemical and physical systems associated with agricultural and livestock production. Therefore, it has become necessary to improve the national

strategic intelligence, thus triggering adoption of the national platform for risk analysis of chemical hazards in foods, both from animal and vegetable origin.

4. RENARA

The project of the National Network for Risk Analysis for Food Chemicals (RENARA) aims to meet this need, presenting itself as an anchor project in the portfolio of chemical risk analysis in food. The risk analysis platform is being developed to generate and pre-process data resulting from the evaluation of residues of veterinary medicines and contaminants in food. This will enable the safety of food products to be improved and provide the scientific community, government agencies, entrepreneurs and other stakeholders a tool that demonstrates transparently the control over production processes and product quality.

The strategy will be to map the gaps in knowledge, information and data by establishing a network that will research effects, quantify responses, improve determination methods, establish a set of processes and technologies and set up a database for geo-referenced information.

This database will be structured for information on chemical risk analysis of veterinary products, pesticides and environmental contaminants in foods. Therefore, the proposal is organized into nine Project Components (PC). Among the Projects Components is highlighted PC 3 –Management of Chemical Risk In Food, under the responsibility of the Coordination of Residues and Contaminants (CRC/SDA/MAPA), which aims to develop tools to support and improve the management of chemical risks in food.

For the development of PC 3, the following Action Plans are outlined:

1. Project Management component. Objective: Make the project management component.
2. Establish business rules to support development of the national system for intelligent risk management (Sigri). Objective: Establish business rules in order to support the design of an intelligent system for managing chemical risks in food.
3. Establish a national system of early warning of chemical hazards in food (SINARQ). Objective: Develop, validate and establish an efficient and effective national system of early warning of chemical hazards in foods.
4. Establish a platform for interface data and information for the coordination of risk management in food chemistry. Objective: Establish and build tools and official mechanisms that promote the effective management of chemical risk in food.
5. Establish policies, mechanisms and technical tools that promote the prevention of occurrence and recurrence of non-conformities that lead to chemical hazards in food. Objective: To prevent and minimize the occurrence and recurrence of non-conformities that lead to chemical hazards in food, offering subsidies for the establishment of policy and technical tools and mechanisms for the prevention and management of risk.
6. Establish specific mechanisms for feedback of data and information on risk management to RENARA. Objective: Establish feedback mechanisms to assess and diagnose properly the data and information obtained from the risk management actions aimed at exploring more effective risk management and predict potential chemical risks in food, considering issues of spatio-temporal demand and the effective availability of veterinary products, pesticides and related products.
7. Establish specific mechanisms for chemical risk management in minor crops and animal production chains with lower registered intake of veterinary products. Objective: To manage chemical risks specific to minor crops or CSFIs (crops with insufficient plant health support) and risks to livestock production chains with lower registered intake of veterinary products.
8. Establishing a platform interface for data and information management for the coordination of chemical risk in food during times of SPS (sanitary and phytosanitary) crises or emergencies. Objective: Establish and build tools and official mechanisms that promote the efficient and effective management of

chemical risk in food during times of SPS crises or emergencies, offering subsidies for the implementation of governmental mechanisms of interaction between permanent managers, assessors and risk communicators.

9. Technology transfer. Objective: To disseminate innovative actions in the subject PC.

The directions of RENARA will be duly transmitted to the members of the project portfolio teams, observing their particularities. The management of the project will depend on the feedback of RENARA and the advances and difficulties experienced by the teams involved in proposing studies of the supply chains and Brazilian regions. At the same time, the data already available in different official organs of the government are properly validated and refined for use in risk analysis.

At the end of the project, the main expected outputs are: set and applied models; database of chemical hazards in food; established and systematized risk analyzes; network of trained and accredited laboratories with an innovative set of methods and sampling procedures; and availability of analytical and managerial methodologies. All these results converge in a network operating at the frontier of knowledge, established in sovereign character, effective and enduring and empowered to deal with and resolve, in light of the best available science and techniques, each and every problem classified as priority regarding the topic.

5. CONCLUSION

The monitoring of residues and contaminants in foods in Brazil is performed by the PNCRC, which provides the necessary system guarantees for the monitoring of foods produced in Brazil. With the advent of RENARA, Brazil gains a robust tool for identifying hazards and risks associated with the presence of residues and contaminants, enabling the development of public policies and guidelines based on risk analysis in order to continuously provide food safety for the Brazilian population and consumers of Brazilian food worldwide.

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IDENTIFICATION AND ASSESSMENT OF EMERGING ISSUES ASSOCIATED WITH CHEMICAL CONTAMINANTS IN DAIRY PRODUCTS

L. D. Feijó, M. S. Fleury, A. J. Portz, R. L. Castelo Branco, R. S. Rocha and A. M. S. Silva

ABSTRACT

The Brazilian Ministry of Agriculture, Livestock and Supply has expanded its monitoring of residues of antibiotics, antiparasitics and other substances in animal products in order to identify whether the levels of such substances are at safe concentrations for human consumption. A new national program (RENARA) for identifying and managing the risks associated with the presence of residues and contaminants in food is outlined.

Keywords: Antimicrobial, Antiparasitic, Contaminant, Dairy, Food safety, Milk, Risk analysis

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IDF's conventions on spelling and editing should be observed. See Annex 1.

ANNEX 1

IDF CONVENTIONS ON SPELLING AND EDITING

In the case of native English speakers the author's national conventions (British, American etc.) are respected for spelling, grammar etc. but errors will be corrected and explanation given where confusion might arise, for example, in the case of units with differing values (gallon) or words with significantly different meanings (billion).

| | |
|--|---|
| “ | Usually double quotes and not single quotes |
| ? ! | Half-space before and after question marks, and exclamation marks |
| ± | Half-space before and after |
| microorganisms | Without a hyphen |
| Infra-red | With a hyphen |
| et al. | Not underlined nor italic |
| e.g., i.e.,... | Spelled out in English - for example, that is |
| litre | Not liter unless the author is American |
| ml, mg,... | Space between number and ml, mg,... |
| skimmilk | One word if adjective, two words if substantive |
| sulfuric, sulfite, sulfate | Not sulphuric, sulphite, sulphate (as agreed by IUPAC) |
| AOAC <u>INTERNATIONAL</u> | Not AOAC! |
| programme | Not program unless a) author is American or b) computer program |
| milk and milk product | rather than “milk and dairy product” - Normally some latitude can be allowed in non scientific texts |
| -ize, -ization | Not -ise, -isation with a few exceptions |
| Decimal comma | in Standards (only) in both languages (as agreed by ISO) |
| No space between figure and % - i.e. 6%, etc. | |
| Milkfat | One word |
| USA, UK, GB | No stops |
| Figure | To be written out in full |
| 1000-9000 | No comma |
| 10 000, etc. | No comma, but space |
| hours | ∅ h |
| second | ∅ s |
| litre | ∅ l |
| the Netherlands | |
| Where two or more authors are involved with a text, both names are given on one line, followed by their affiliations, as footnotes | |
| for example | A.A. Uthar ¹ & B. Prof ² ¹ University of ² Danish Dairy Board |

IDF does not spell out international organizations

INTERNATIONAL DAIRY FEDERATION / FEDERATION INTERNATIONALE DU LAIT
Boulevard Auguste Reyers, 70/B - 1030 Brussels (Belgium) - <http://www.fil-idf.org>