The limitation of legislations and shortage in implementation of regulatory measures regarding the uses of antimicrobials especially in developing countries, pay the attention of Scientists and UN organizations (FAO, OIE and WHO) to address the issues related to antimicrobial use/misuse, the emergence of resistant pathogens and the potential public health impact. As a scientists and being previously Expert Consultant for FAO, OIE and WHO of the UN, <sup>(1)</sup> we have concluded the following in this regard.

### Antimicrobial resistance:

Today, development and spread of antimicrobial resistance has become a global public health problem that is impacted by both human and non-human antimicrobial usage. The consequences of antimicrobial resistance in bacteria causing complicated human infections include:

(1) Increased frequency of treatment failures and increased severity of infection which may be manifested by prolonged duration of illness, increased frequency of bloodstream infections, increased hospitalization, or higher mortality.

(2) Antimicrobial agent use in humans disturbs the microbiota of the intestinal tract, placing such individuals at increased risk of certain infections. Individuals taking an antimicrobial agent, for any reason, are therefore at increased risk of becoming infected with pathogens resistant to the antimicrobial agent. <sup>(2)</sup>

### Resistant bacteria & Resistance genes:

Development and spread of antimicrobial resistance as a consequence of exposure to antimicrobial agents is widely documented in human medicine. Transfer of R Plasmid and emergence of new drug resistance gene cassettes have been reported in human. Typical transferable resistance determinants are those conferring resistance to sulphonamide, tetracycline, trimethoprim, and streptomycin. It is generally acknowledged that, any use of antimicrobial agents can lead to the emergence of antimicrobial resistant microorganisms and further promote the dissemination of resistant bacteria and resistance genes. Furthermore, resistance genes neither respect phylogenetic, geographical nor ecological borders. Thus, the use of antimicrobials in one area, can have an impact on the resistance situation in another area and resistance problems in one country can spread to another country. <sup>(3)</sup>

#### Antimicrobial residues:

Antimicrobial usage for the treatment of bacterial diseases can result in residues of antimicrobials. The public health risk associated with antimicrobial residues depends on the quantity of the antimicrobial encountered or consumed. If present in concentrations above the established maximum residue limits, or if the drug is used without appropriate authorization based on scientific assessment of the benefit and risk of the treatment, residues can present a hazard to human health. <sup>(4)</sup>

### Toxicological aspects:

Concerns have been expressed about the genotoxicity of some antibiotics as chloramphenicol and its metabolites, its embryo- and fetotoxicity, its carcinogenic potential in humans and the lack of dose response relationship for aplastic anemia in humans.

Drug allergies are generally considered to be type 1 immune response mediated through IgE. Symptoms include urticaria, angioedema and might include anaphylaxis.<sup>(5)</sup>

# Effects of antimicrobial residues on human intestinal flora through;

- (i) Exerting a selective pressure on the dominant intestinal flora;
- (ii) Favoring the growth of micro-organisms with natural or acquired resistance;
- (iii) Promoting the development of acquired resistance in pathogenic enteric bacteria;
- (iv) Impairing colonization resistance; or
- (v) Altering metabolic enzyme activity of the intestinal microflora.<sup>(6)</sup>

## Data gaps and future research needs; There is a need for;

- More national data on prevalence of antimicrobial resistance in various bacteria.
- Better national data on usage of different antimicrobials.
- More national data on the occurrence of residues of various antimicrobials.
- More knowledge on spread of resistance genes to human pathogens.
- Better methods to determine the effects of antimicrobials residues on intestinal microflora.
- More research about pharmacological and pharmacokinetical aspects of antimicrobials used.

## Need to support and assist national capacity building in their efforts regarding;

- Implementation of preventive measures (hygiene, environmental conditions, and vaccines);
- · Strict follow up of prudent use guidelines;
- · Regulatory control of antimicrobial usage; and
- Monitoring of antimicrobial use and antimicrobial resistance.

### **Recommendations:**

- Measures to prevent the spread of antimicrobial resistance should be developed.
- Regulatory systems to prevent the occurrence of antimicrobial residues should be encouraged.
- Studies to assess the likelihood of gene transfer should be implemented.
- Capacity to monitor the usage of antimicrobial agents should be built up.

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