

BIOTECHNOLOGY AND ITS APPLICATION TO VETERINARY SCIENCE

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Summary: *A questionnaire was sent to the 29 Member Countries of the OIE Regional Commission for the Americas and information and comments were received from the Delegates of 21 Member Countries. The questionnaire covered aspects relating to the application of biotechnology to animal health, especially prevention-related issues, including: the development and production of medicinal products and vaccines; the use of metabolic modifiers, probiotics and prebiotics; advanced veterinary diagnostic methods; immunocastration and other applications. The questionnaire also covered the aspects of regulations and public perceptions.*

The report analyses the situation in the countries of the region in relation to the state of the art in these technologies worldwide, revealing that modern biotechnology-based technologies offer huge potential for the production of vaccines, medicinal products and other veterinary products.

The development and use of these technologies is concentrated in a few countries of the region, while in others they are still not in widespread use. This creates the need to publicise and provide training in these technologies, for which suitable development conditions exist in a number of countries in the region. It is also necessary to foster the establishment of a comprehensive and effective regulatory framework for the safe use of these technologies from the dual standpoint of biosafety and of the regulations established in the veterinary register. All the countries of the region consider that it is important for the OIE to issue additional standards for the production of veterinary products using modern biotechnology.

Key words: biotechnology – veterinary science – Americas

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Introduction

A technical item on the 'Application of Genetic Engineering for Livestock and Biotechnology Products' was presented and analysed at the 73rd General Session of the OIE in May 2005, based on the precept that modern agricultural biotechnology applied to animal health and production is a fascinating mix of animal science, veterinary medicine and molecular biology.

On that occasion, the emphasis was placed on important issues such as regulations and public perceptions of applying biotechnology to animal health and production, especially such controversial issues as animal transgenesis, cloning or xenotransplantation.

Both the results of the questionnaire circulated for the technical item and the technical presentation itself provided important and extremely useful input for the work of the OIE and its Member Countries.

For the upcoming Conference of the OIE Regional Commission for the Americas, the presentation and analysis will be on the application of biotechnology to animal health, especially prevention-related subjects such as the development and production of medicinal products and vaccines, immune boosters for farm animals and aquatic organisms (including metabolic modifiers, prebiotics and probiotics), advanced veterinary diagnostic methods, immunocastration, etc. The questionnaire also covers the aspects of regulations and public perceptions.

To obtain information from the member countries on this technical item, a questionnaire was circulated on the main issues involved.

Answers were received from 21 Member Countries (Argentina, Barbados, Belize, Brazil, Canada, Chile, Colombia, Cuba, Dominican Republic, Ecuador, El Salvador, Guatemala, Guyana, Haiti, Honduras, Mexico, Panama, Paraguay, Trinidad and Tobago, United States of America and Uruguay).

In a summary report such as this, it is not possible to cover the full range of potential biotechnology applications to veterinary science. We have therefore selected a group of technologies with internationally-acknowledged real or potential impact whose use in the region should be promoted and regulated.

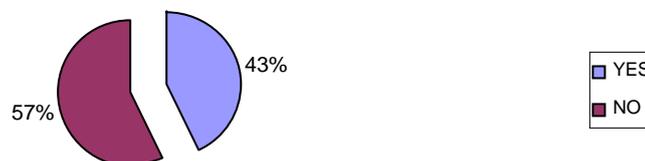
The report has been divided into the following eight sections covering the state of the art and application of these leading modern biotechnology applications to veterinary science in relation to the region's current stage of development, based on the answers to the questionnaire:

1. Research;
2. Biotechnology-derived veterinary vaccines;
3. Immunocastration;
4. Growth promoters and/or immune boosters;
5. Veterinary diagnostic systems;
6. Prebiotics and probiotics;
7. Chief shortcomings of biotechnology applications to veterinary science in each country;
8. Regulatory framework.

1. Research

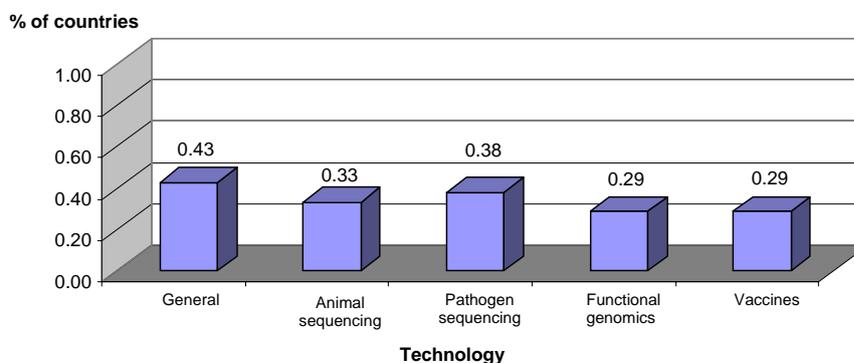
Some countries in the region have a highly developed research capacity in this field, most of which is concentrated in Argentina, Brazil, Canada, Chile, Colombia, Cuba, United States of America, Mexico and Uruguay. These countries represent 43% of the countries that answered the questionnaire (see [Figure 1](#)).

Figure 1.– Is your country conducting research into animals and animal products, including vaccines and medicinal products that have been obtained using biotechnology?



A number of these countries even have research capacity in advanced fields such as genomics, proteomics and bioinformatics applied to veterinary science (see [Figure 2](#)).

Figure 2.– Is your country conducting research into animal genomics (including functional genomics, proteomics and bioinformatics)?



While it is true that the absence of major research activities in this field in more than half the countries in the region is not a favourable factor, the existence of these hubs of biotechnology development applied to veterinary science opens up real opportunities for training, technology transfer and support for the development of infrastructure and specific projects in the region.

2. Biotechnology-derived veterinary vaccines

It has been amply demonstrated that vaccination is the best available method for preventing economic losses in animals with a good cost/benefit performance. Nevertheless, several regions of the world, including our own, continue to suffer from serious diseases.

Eight of the 10 leading causes of death in humans are attributed to infectious diseases. In animals, which have a shorter life span, the situation is even worse.

Conventional vaccines have already been used for more than two centuries. They will continue to be used just as extensively in cases where they are the most effective vaccines available and will continue to be developed where appropriate in other cases.

However, a number of different vaccines produced using biotechnology are already in use and many more are at different stages of development. Their benefits include decreasing the risk of reversion to virulence of live vaccines and of interference with antibodies induced by passive immunisation, avoiding contamination with other viruses, reducing damage during storage and other aspects [1, 6, 13].

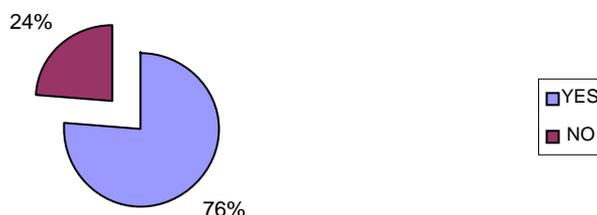
The great advantage of these vaccines is that they can be used in systems for differentiating infected from vaccinated animals (Differentiate Infected from Vaccinated Animals – DIVA) [5].

As DIVA vaccines make it possible to differentiate vaccinated animals from animals exposed to virus strains, they allow diseases to be eradicated from a country much faster and more economically than by using conventional eradication methods. One of the first diseases to be successfully eradicated using the DIVA strategy was Aujeszky's disease.

Biotechnology-derived veterinary vaccines are being used not only to control infectious diseases, but also to increase productivity by modulating hormones or immune system functions, as well as for immunocastration, ectoparasite control, etc.

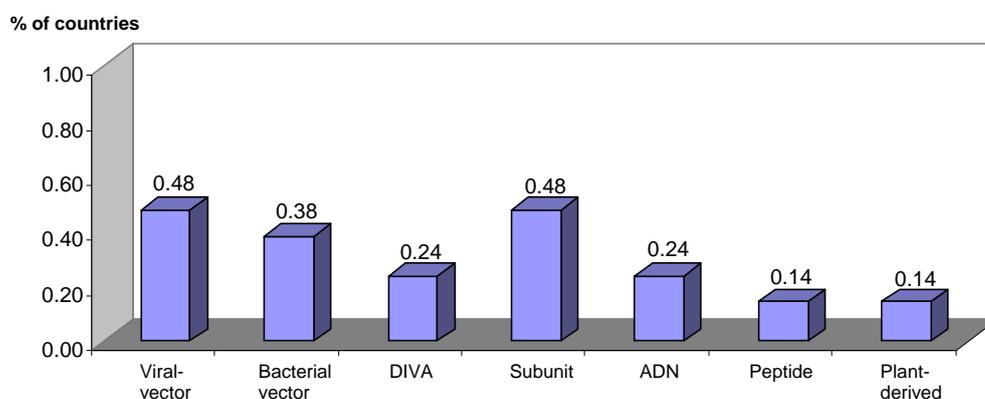
Of the countries in the survey, 76% produce or administer some sort of biotechnology-derived vaccine, which is a significant step forward in the introduction of biotechnology ([Figure 3](#)).

Figure 3.– Does your country produce or administer any animal vaccines obtained using biotechnology?



As regards the technologies used, unfortunately only a quarter of the countries use at least one of the marker vaccines allowing differential diagnosis ([Figure 4](#)).

Figure 4.– Vaccine types



An important aspect of these new technologies is their safe use and adequate public information about their nature and benefits, regulatory scrutiny of each technology and how the technologies are managed to reduce their potential risks to a minimum.

Poor management of information for the general public and policy-makers can lead to failure or a ban on a product that is demonstrably safe and effective.

[Figure 5](#) shows that information is inadequate in two thirds of the countries in the region, and [Figure 6](#) shows that in only one quarter of the countries is the public informed and considers them to be safe.

This is a matter to which we must pay due attention if we wish to take advantage of the enormous potential of these technologies on a safe regulatory basis.

Figure 5.– Has the public been informed that biotechnology-derived vaccines or medicinal products are used in your country?

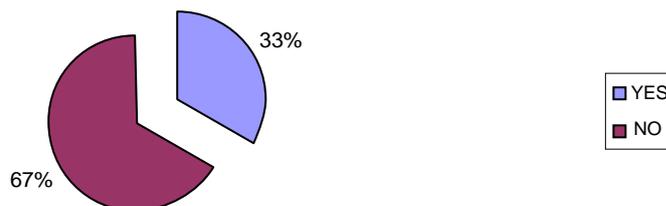
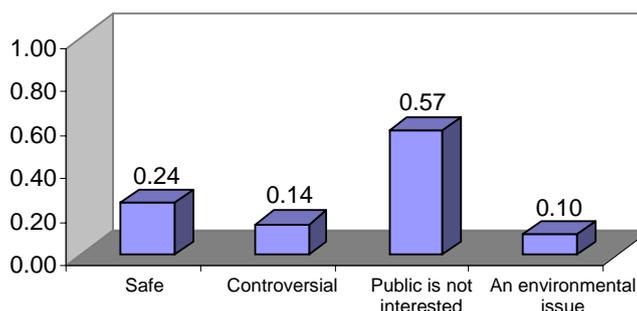


Figure 6.— How does the public in your country generally perceive biotechnology-derived vaccines and/or medicinal products?



3. Immunocastration

It is common for economically important animals (pigs, cattle) and pets (dogs, cats) to be prevented from breeding.

The most frequently used methods are surgical castration and the administration of steroids. Both these methods have drawbacks. Surgical castration must be performed by specialist personnel, is irreversible, causes infections and can later lead to inguinal hernias and immunosuppression, in some cases resulting in death. The administration of steroids causes side effects detrimental to animal health.

For these reasons, animal immunocastration has been tested using peptides similar to gonadotropin-releasing hormone (GnRH), combined with proteins, to trigger antibodies that neutralise the function of GnRH [11].

Immunocastration is reported to be an advantageous alternative in economically important animals, to improve the aggressive behaviour of males, the smell and taste of meat and feed conversion, to produce leaner carcasses and to reduce the consumption of animal feed.

In the case of pets, the reversibility of immunocastration is an advantage that differentiates it from the other alternatives.

Fewer than half the countries in the region use immunocastration and in only 18% of these countries is the public informed about its potential, its use and the regulations that guarantee the safe use of immunocastration technology.

A point of note is that this technology is considered controversial in only 10% of the countries.

4. Growth promoters and/or immune boosters

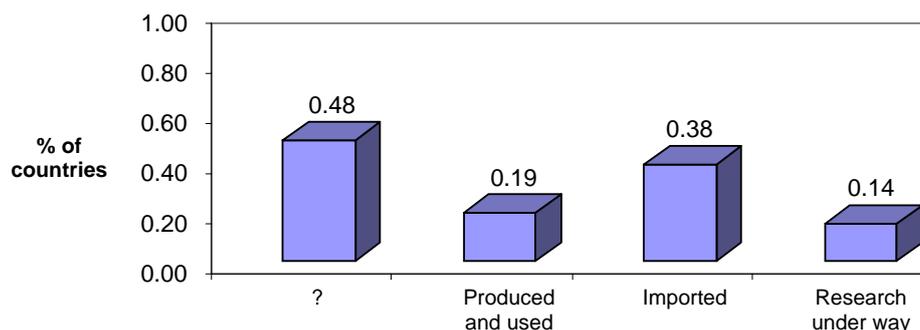
In recent years, biomolecules have been developed that have proven effective in inducing endogenous genes that promote growth and boost the immune system (innate and acquired immunity).

Not only does this triggering of various metabolic pathways foster the growth and development of young animals, it also increases rates of survival, weight gain and synchronisation of the animal population.

Metabolic modifiers have been tested with particular success in aquatic organisms (fish and shrimp) and been found to significantly improve production and to reduce the use of antibiotics and chemicals [7].

Even though it is a fairly recent application, 48% of the countries in the region are already using or researching growth promoters and/or immune boosters (Figure 7).

Figure 7.– Does your country produce, administer or conduct research into growth promoters or immune boosters for animals (including aquatic organisms)?



5. Veterinary diagnostic systems

Numerous methods have been used to detect and identify diseases and diagnose their causal agents, ranging from the most conventional methods using morphological and biochemical techniques to an increasing number of immunological and molecular techniques from modern biotechnology.

These immuno-enzymatic techniques are being continually improved and incorporate technologies such as rapid diagnostic strip tests, which are very easy to use, even at production-unit level, and yield an immediate result.

Furthermore, the development of molecular biology has opened up huge possibilities in diagnostic techniques which are fast becoming widespread in veterinary diagnostic laboratories [9].

Single DNA sequences provide a high degree of specificity in the diagnosis and control of pathogenic microorganism species and subspecies, and polymerase chain reaction (PCR) techniques permit extremely high specificity levels [4].

Not only have molecular methods increased the sensitivity and specificity of diagnostic methods, they have also significantly reduced the subjectivity inherent in the interpretation of morphological and biological data.

Real-time polymerase chain reaction (RT-PCR) is one of the latest improvements in PCR techniques to have been incorporated by veterinary diagnostic laboratories. The entire process takes place in an individual sealed tube, which greatly reduces the problem of cross-contamination, and the ability to electronically process the detected fluorescence in real time obviates the need for subsequent reaction and the electrophoretic run required in traditional PCR.

In addition, RT-PCR permits the use of quantitative methods.

The sequencing of complete genomes of pathogens yields major elements for biological studies and for improving parasite diagnosis and control.

The new microarray techniques allow screening for the genotypes of specific parasites and provide major support for epidemiological surveys of veterinary parasites.

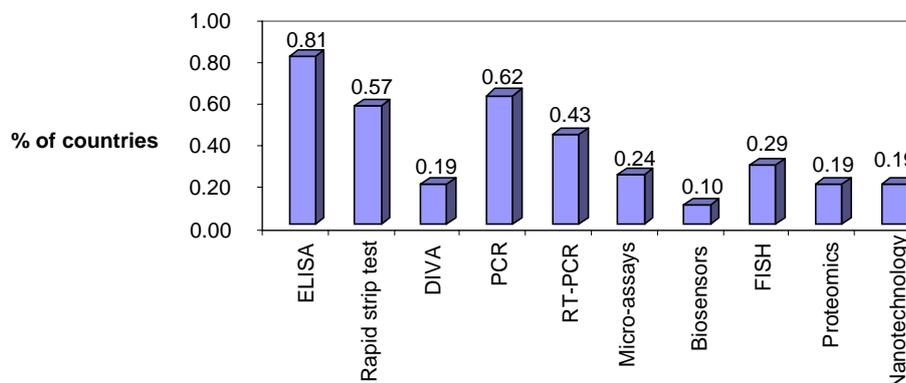
Proteomic techniques make it possible to identify and characterise the proteins produced by pathogens and are of enormous interest to veterinary diagnosis, enabling the protein expression pattern of viruses, bacteria and other pathogens to be studied. Proteomics also allows the study of proteins that are expressed or repressed differentially as a result of being attacked by pathogens, which is extremely important for identifying new methods for using vaccines, medicinal products or other means to control pathogens.

Other technologies such as biosensors, fluorescent in situ hybridisation (FISH) and nanotechnologies are being incorporated as new veterinary diagnostic tools.

The answers to the questionnaire reveal that 80% of the countries in the region produce or conduct research into veterinary diagnostic systems.

However, as [Figure 8](#) shows, only a small percentage of countries report that they use modern molecular biology technologies in veterinary diagnosis, even technologies now considered routine, such as PCR and RT-PCR.

Figure 8.– Diagnostic technologies used in the various countries



6. Probiotics and prebiotics

Probiotics are defined as cultures of live microorganisms that lodge in the intestinal tract of humans and/or animals where they exert a beneficial action on the host's health. The most important genera of probiotic bacteria are *Lactobacillus* and *Bifidobacterium*. Some yeasts also exert a probiotic effect.

Prebiotics are food ingredients that improve the host's health by selectively stimulating the growth and/or activity of probiotic bacteria in the intestinal tract. The leading prebiotics are non-digestible oligosaccharides, including: fructo-oligosaccharides (FOS), galacto-oligosaccharides (GOS), malto-oligosaccharides (MOS) and xylo-oligosaccharides (XOS). The most typical prebiotics are FOS and inulin and they are sold widely for use in humans and monogastric animals.

Symbiotics are a combination of probiotics and prebiotics that have a beneficial effect on the host's health by improving the survival and implantation of probiotics in the gastrointestinal tract by selectively stimulating their activity and/or growth.

Scientific literature documents that the consumption of probiotics, prebiotics or symbiotics improves the intestinal flora, prevents and rehabilitates diarrhoeal diseases, improves the composition of blood lipids, reduces cholesterol, improves blood pressure, increases calcium absorption and retention, modulates immune functions and reduces the risk of colon cancer [3,10,12].

In livestock, the use of probiotics, prebiotics or symbiotics provides the additional benefit of reducing or eliminating the prophylactic use of antibiotics in feed or water.

Widespread use is made of probiotics in aquaculture, where they are used for a number of purposes:

- Competitive exclusion of pathogens;
- Source of nutrients and of enzymes to aid digestion;
- Improvement of water quality;
- Stimulate the immune response;
- Antiviral effects.

Although they have become an important management tool, their effectiveness relies on understanding the competition between the strains used (2).

Two thirds of the countries in the region use such products, mainly in cattle, pigs and poultry, and their increased use should be promoted among the remaining third (Figures 9 and 10).

Figure 9.

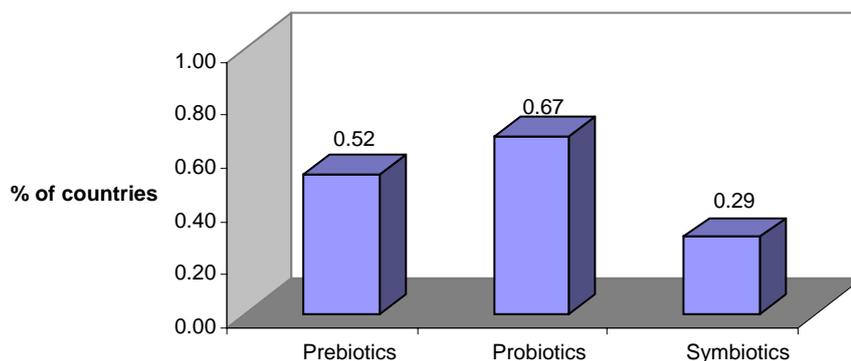
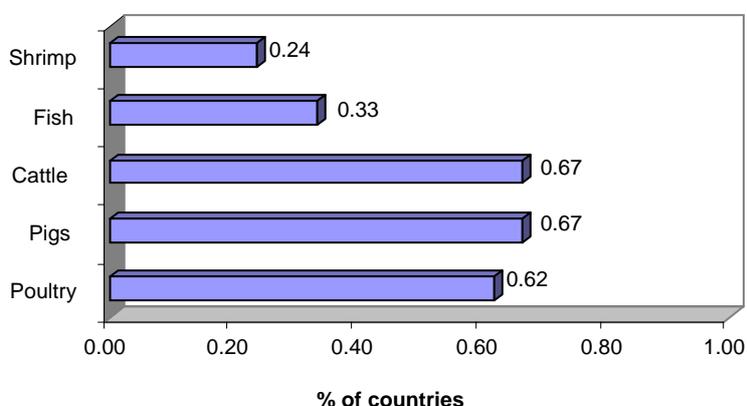


Figure 10.– Species



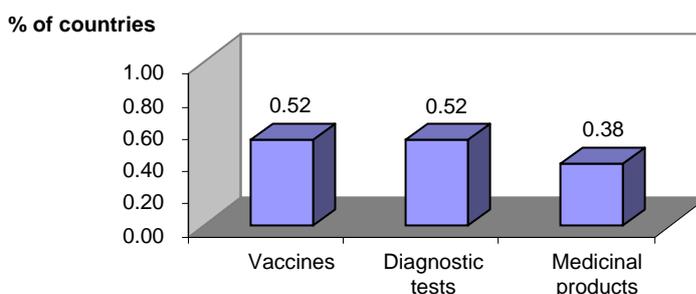
7. Chief shortcomings of biotechnology applications to veterinary science in each country

Three quarters of national veterinary authorities stated that they needed new and more effective biotechnology-based veterinary applications (Figure 11).

A point of note is that, of the countries with the highest level of biotechnology-based veterinary applications, 100% said that they needed new products and that all the delegates that did not say they needed new products had very few biotechnology-based applications in use in their country.

This proves that the more these technologies are known, tested and evaluated, the more possibilities they are found to offer, which means that there is a need to publicise this subject and to train the region's specialists in it.

Figure 11.– What are your country's shortcomings as regards biologics produced using modern biotechnologies to improve the control of animal diseases?



8. Regulatory framework

The preceding sections of this report clearly reveal the huge potential that modern biotechnologies offer veterinary science and we have evaluated the application status of these technologies in the countries of the region.

These technologies require an adequate regulatory framework to guarantee their safe use.

In the case of technologies involving the release of genetically modified organisms (GMOs) into the environment, in addition to the tests required to register any veterinary product (e.g. tests for purity, safety, potency and efficacy), a special risk assessment must be conducted to prove that the product is harmless to human and animal health and is environmentally friendly.

In many instances, the lack of knowledge or of specific regulations leads to a mistaken belief that all modern biotechnology applications are GMOs, but in most cases this is not true.

There are many examples, such as subunit vaccines containing only proteins as the active pharmaceutical ingredient, metabolic modifiers containing only proteins or parts thereof (polypeptides), prebiotics and probiotics, specific diagnosis systems, and so on.

In fact, the majority of the applications covered in this report do not entail the release of genetically modified organisms into the environment.

Where products really are GMOs, they must comply with two sets of regulations, one covering veterinary products as a whole, and the other a set of specific biosafety regulations.

Where genetic engineering techniques are used during the production process but are not contained in the final product, biosafety regulations apply to the place of manufacture but not to places of final use.

The unbridled growth in these technologies calls for the rapid and efficient development of specific regulations for their use, with the situation complicated by the hundreds of companies lobbying for the technologies to be introduced so that they can obtain economic benefits.

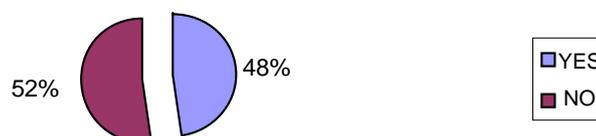
Much progress has been made in the region with regulations for the registration and control of veterinary products to ensure that products are of the proper quality and purity, efficacy and safety and to ensure that treated animals are harmless to consumers.

In addition to the regulations established by national authorities, a admirable drive for regional harmonization is being spearheaded by the Committee of the Americas for Veterinary Drugs (CAMEVET), which is based in the office of the OIE Regional Representation for the Americas [8].

The survey results corroborate CAMEVET's finding that progress needs to be made with the regulatory framework of veterinary products derived from modern biotechnology.

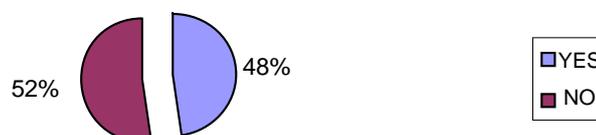
Fewer than half the countries in the region that answered the survey have biosafety regulations for the use of these technologies ([Figure 12](#)).

Figure 12.– Do biosafety regulations exist for biotechnology-derived vaccines?



Another point of equal concern is that fewer than half the countries have special requirements for the registration of biotechnology-derived veterinary medicinal products ([Figure 13](#)).

Figure 13.– Are there any special requirements for registering biotechnology-derived vaccines?



Clearly there is an urgent need to support the countries of the region in the implementation of a proper regulatory framework for the safe use of these technologies, from the standpoints of both biosafety and veterinary product registration.

Therefore it is hardly surprising that the only question in the survey to elicit a unanimous yes from all the countries in the region was the idea that the OIE should issue additional standards in the field of veterinary products derived from modern biotechnology.

Conclusions

1. Technologies based on modern biotechnology offer enormous potential for the production of vaccines, medicinal products and other veterinary products.
2. The development and use of these technologies is concentrated in a few countries of the region, while in others they are still not in widespread use.
3. There is a need to publicise and provide training in these technologies, for which suitable development conditions exist in a number of countries in the region.
4. It is necessary to foster the establishment of a comprehensive and effective regulatory framework for the safe use of these technologies from the dual standpoints of biosafety and the regulations established in the veterinary register. The member countries deem it necessary for the OIE to issue additional standards in this field.

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