REPORT OF THE MEETING OF THE OIE AD HOC GROUP ON BIOTECHNOLOGY

Paris, 26–28 August 2008

A meeting of the OIE ad hoc Group on Biotechnology was held at the OIE Headquarters in Paris from 26 to 28 August 2008. The meeting was chaired by Prof. Sándor Belak. Dr Cyril G. Gay acted as rapporteur. The Agenda and List of Participants are given at Appendices I and II, respectively. This was the last meeting of the OIE ad hoc Group on Biotechnology in its current format.

1. Introduction

The ad hoc Group on Biotechnology was welcomed by Dr Gideon Brückner, Deputy Director General, OIE, on behalf of Dr Bernard Vallat, Director General of the OIE.

Dr Brückner identified the task of the ad hoc Group for the current meeting:

• To discuss and propose Terms of Reference for the formation of two new ad hoc Groups to focus on diagnostics and vaccines related to new and emerging biotechnologies.

The ad hoc Group was encouraged not to focus too much of its time on background papers as its main focus should be to consider issues related to biotechnology that would eventually be adopted as chapters or guidelines for inclusion in either the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (Manual Terrestrial) or Terrestrial Animal Health Code (Terrestrial Code). However, should the information or current knowledge on a specific subject not be sufficient to guide the discussions, the Group should feel free to request a supporting background paper. The ad hoc Group in reviewing the Terms of Reference for the ad hoc Groups on diagnostics and vaccines should identify priority areas that could be developed into guidelines for OIE Members.

2. List of priority topics for future consideration by the OIE

The ad hoc Group discussed and agreed on the direction provided by Dr Brückner, and identified the following topics that should also be considered by the OIE.

Following an e-mail message sent in July by one member of the Group regarding cloned and transgenic animals, a detailed discussion followed. The Group resolved the following points:

• The ad hoc Group respects the direction set by the Biological Standards Commission, i.e. that it should focus on molecular diagnostics and vaccinology, however, the Group believes that cloned and transgenic animals should not be ignored by OIE.

• In the context of animal health, the technologies used to produce clones and transgenic animals are at the core of biotechnology.

• The development of cloning and transgenesis is currently quite advanced in various developing and developed countries. In addition, international movements to further develop these technologies are beginning to occur. Indeed, commercial ventures are now among the stakeholders attracting the attention of national regulatory bodies. Such developments have several facets including breeding traits (such as disease-resistant animals, special products for nutritional purposes [milk, meat, etc.], and novel products particularly for pharmaceutical use) or other traits.
• New breakthroughs in these technologies, such as targeted manipulation of the zygote, will increase further the number of applications.

• These reproductive biotechnologies imply inter-relationships with a number of issues ranging from traceability (see cloned livestock monitoring systems) to welfare, health, food safety, and the risks from pathogens associated with cloned and transgenic animals either as individuals or embryos. This includes, for example, transgenic animals that failed to express the targeted function but that can be numerous and susceptible to becoming a candidate for entrance to the livestock production and later the food chain.

Hence there is a clear need for IGOs\(^1\) to develop guidelines as has been requested by the Codex Task Force, and the OIE could be the ideal organisation to do so. It is fortunate that the industry, as seen during a recent meeting of the IETS\(^2\), holds such a view, but it needs to be further discussed and approved by the OIE.

Resolution XXVIII adopted by the International Committee during the 73rd General Session in May 2005 recommended that the OIE should consider this as a priority issue. The Group recognises that a horizontal approach is needed, involving several OIE Specialist Commissions and at least two departments of OIE. It was suggested that a horizontal \textit{ad hoc} Group be established responsible for the many items involved with such animals either as zygotes/embryos or as living individuals.

3. Future work plan and Terms of Reference for the two proposed \textit{ad hoc} Groups

The draft of Terms of Reference provided by the OIE was reviewed by the \textit{ad hoc} Group.

The \textit{ad hoc} Group recommends that the current \textit{Terrestrial Manual} Chapter 1.1.7 Biotechnology in the diagnosis of infectious diseases and vaccine development, be separated into two new chapters, one on new and emerging diagnostic technologies that would be managed by the new \textit{ad hoc} Group on Molecular Diagnostic Tests, and the other on vaccine technologies for innovative applications that would be managed by the new \textit{ad hoc} Group on Vaccinology.

The new chapter on new and emerging diagnostic technologies should integrate part of Chapter 1.1.5 Validation and quality control of polymerase chain reaction (PCR) methods used for the diagnosis of infectious diseases, and the parts of chapter 1.1.7 that specifically address diagnostics.

The new chapter on vaccine technologies for innovative applications should integrate relevant information in the current chapter 1.1.7 and Chapter 1.1.8 Principles of veterinary vaccine production, as appropriate. The new chapter should initially focus on the following three applications: 1) vaccines for disease control in domestic animals; 2) vaccines for food safety; and 3) vaccines for wildlife.

Where applicable, the \textit{Manual of Diagnostic Tests for Aquatic Animals} should reference the new chapters.

3.1. \textit{Ad hoc} Group on Molecular Diagnostics

The \textit{ad hoc} Group recommended that the Terms of Reference for the \textit{ad hoc} Group on Molecular Diagnostics be as follows: develop guidelines for new technologies that have current and relevant applications for early disease detection, surveillance, and recovery from disease outbreaks to enable the transfer of these molecular diagnostic technologies to OIE Reference Laboratories and national veterinary laboratory networks.

Criteria that should be taken into consideration when determining whether a new diagnostic technology is ready and in need of an OIE guideline would be that the technology has a specific application (e.g. early detection) and that it has been validated to at least the bench level.

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1 IGO: Inter-governmental organisations
2 IETS: International Embryo Transfer Society
The following new molecular diagnostic methodologies were identified:

**Direct diagnostic assays**

- PCR-based assays
  - Real time;
  - Rapid detection in a disease outbreak;
  - Multiplex;
  - PCR robotics.
- Isothermal amplification assays;
- Microarray technologies;
- Rapid sequencing technologies, phylogenic analysis/bioinformatics;
- Genomic technologies to determine virulence;
- Complete full length genome sequencing technologies;
- Pen-side test technologies (lateral flow devices);
- Portable PCR technologies for field use;
- Nanotechnology;
- Proximity ligation technologies;
- *In-situ* hybridisation;
- Proteomics (detection of proteins).

**Indirect diagnostic test (antibody-based assays)**

- Bioluminometry;
- Fluorescence polarisation;
- Chemoluminescence technologies;
- Biosensors;
- Biomarkers;
- Recombinant proteins;
- Synthetic proteins;
- Improved monoclonals for enzyme-linked immunosorbent assays (ELISA).

Applications of these new molecular diagnostics include, but are not limited to, the following: 1) disease surveillance; 2) early detection; 3) detection during an outbreak; 4) detection during the recovery phase (to regain OIE disease-free status); 5) molecular epidemiological investigations; 6) implementation of DIVA\(^3\) strategies.

In addition, these technologies will have important applications in the identification of clinical parameters for use in animal production and animal welfare, such as phenotypes (including non-infectious diseases), physiological conditions, and genotypes.

The *ad hoc* Group identified the priority topics that will benefit from guidelines by experts on the *ad hoc* Group on molecular diagnostics:

**a) Early detection and identification**

- PCR-based technologies
  - Issues:
    - Strategies to identify the most appropriate sequences for the purpose intended;
    - Positive results and test interpretation.
- Isothermal nucleic acid detection technologies
  - Issues:
    - Instrumentation;
    - Further development is required;
    - Positive results and test interpretation;
    - Bench and field validation is required.

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3 DIVA: Differentiating infected from vaccinated animals
• Microarrays
  o Issues:
    • Instrumentation;
    • Further development is required;
    • Positive results and test interpretation;
    • Reproducibility;
    • Increase detection sensitivity;
    • Bench and field validation is required.

• Nanotechnologies
  o Issues:
    • Nanoparticle residues in \textit{in vivo} diagnostic testing;
    • Characterisation of the nanomaterial;
    • Instrumentation.

• Rapid sequencing technologies
  o Issues:
    • Instrumentation;
    • Sample information;
    • Building genome databases;
    • Data processing (validation of software);
    • Sharing sequencing data;
    • Harmonisation of data.

• Complete full-length genome sequencing technologies (e.g. metagenomics for previously unidentified and emerging pathogens)
  o Issues:
    • Instrumentation;
    • Sample information;
    • Data processing;
    • Bioinformatics.

b) DIVA diagnostics

• Improved monoclonals and recombinant proteins
  o Issues:
    • Sensitivity;
    • Specificity;
    • Link with vaccine discovery to identify appropriate markers;
    • Field validation.

• PCR-based technologies
  o Issues:
    • Identification of unique sequences to differentiate live vaccine strains from wild-type pathogens;
    • Field validation.

c) Rapid detection in the field (pen-side of flock-side tests)

• Pen-side test technologies (lateral flow devices)
  o Issues:
    • Sensitivity;
    • Specificity;
    • Detection range.

• Portable PCR technologies for field use
  o Issues:
    • Field validation;
    • DIVA applications.

• Isothermal technologies
  o See above.
d) Molecular epidemiology for tracing routes of infections

- Rapid sequencing technologies, phylogenetic analysis/bioinformatics
  - Issues:
    - Identification of useful sequences;
    - Identification of correct samples;
    - Data processing.

3.2. Ad hoc Group on Vaccinology

The ad hoc Group recommended that the Terms of Reference for the ad hoc Group on Vaccinology, which would include the use of various types of vaccines and their implications for animal and public health, be as follows: to develop guidelines for new vaccines that have been specifically designed for disease control, food safety, and wildlife, including all aspects of efficacy, potency, safety, and purity (i.e. quality) as well as the risk assessment of the release of biotechnology-derived vaccines and the food derived from animals vaccinated with these vaccines.

Criteria that should be taken into consideration when determining whether a vaccine technology is ready and in need of an OIE guideline are those technologies that have achieved proof-of-concept in a target host animal species and sufficient published information is available.

Where applicable, the ad hoc Group on Vaccinology should take into consideration guidelines from relevant international standard-setting bodies.

The following vaccine technologies were identified as needing new or improved guidelines:

- DNA vaccines (completed);
- Reverse genetics;
- Chimerics;
- Gene-deleted vaccines;
- Marker vaccine technologies (DIVA vaccines);
- Recombinant vectors;
- Virus like particles;
- Nanotechnology (nanoemulsions);
- Adjuvant formulations for targeted immune responses.

The ad hoc Group identified the priority topics that will benefit from these new technologies and recommended the preparation of the following guidelines by experts on the ad hoc Group on Vaccinology:

**Vaccines for disease control**

- Prevention of pathogen transmission;
- DIVA vaccines;
- Delivery systems for mass immunisation;
- Onset of immunity;
- Duration of immunity;
- Cross-protection.

**Vaccines for food safety**

- Efficacy in carrier hosts (e.g. *Escherichia coli* 0157 in cattle);
- Acceptable standards of efficacy specific for the food safety issues;
- Acceptable potency standards.

**Vaccines for use in wildlife worldwide**

1. Classical swine fever;
2. Brucellosis;
3. Tuberculosis;
4. Porcine reproductive and respiratory syndrome (PRRS);
5. Rabbit haemorrhagic disease;
6. Rabies;
7. Immunocastration;
8. The needs are not limited to the above diseases.

4. Review and discussion of drafts of background papers

4.1. Transgenic animal technologies in farm animals

The Group completed a background document on transgenic farm animals authored by Dr Harpreet Kochhar, which could form the basis for a future document on animal health issues associated with this biotechnology (i.e. transgenesis).


No document was presented for review. The Group discussed the possibility of preparing a guideline depending on the review by the OIE of the recommendations in Item 2 above.

4.3. Other background papers as planned at the November 2007 meeting

Reference is made to the November 2007 Report of the ad hoc Group on Biotechnology and the proposed list of guidelines and background papers. The Group offered to prepare any of the documents that do not fall under the scope of the new ad hoc Groups on Molecular Diagnostics and Vaccinology as OIE sees fit.

5. Other Issues

5.1. Follow-up from the International Symposium on ‘Animal Genomics for Animal Health

The proceedings of the Symposium were published in August 2008 and include a Report and ‘Roadmap’ with recommendations as endorsed by the ad hoc Group on Biotechnology. The recommendations include many of the aspects that will be affected by genomics, such as therapeutics (RNA-based technologies), transgenic animals (disease-resistant traits), marker-assisted selection of animals with desirable health and production traits, selection of good responders to vaccination, etc.

At the last meeting, the ad hoc Group endorsed the development of a ‘Roadmap’ and recommendations to advance the use of animal genomics to improve animal health and animal welfare.

The ad hoc Group also recommended that a second International Symposium on Animal Genomics for Animal Health be held to review the progress made with the ‘Roadmap’ and to facilitate future progress.

The ad hoc Group requested OIE guidance on how best to progress the ‘Roadmap’.

5.2. Emerging technologies

Increasingly emerging technologies are being used in the area of therapeutics; for example, nanocarbon molecules are being used to target drugs to specific areas of the body. Once the pharmacological effect has been achieved, the residual nanoparticles must be absorbed or excreted. This may evolve as an area of concern in food-producing animals.
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Agenda

1. Introduction

2. List of priority topics for future consideration by the OIE

3. Future work plan and Terms of Reference for the two proposed ad hoc Groups:
   3.1. Ad hoc Group on Molecular Diagnostics
   3.2. Ad hoc Group on Vaccinology

4. Review and discussion of drafts of background papers
   4.1. Transgenic animal technologies in farm animals
   4.3. Other background papers as planned at the November 2007 meeting

5. Other issues
   5.1. Follow-up from the International Symposium on ‘Animal Genomics for Animal Health
   5.2. Emerging Technologies
Appendix II

MEETING OF THE OIE AD HOC GROUP ON BIOTECHNOLOGY
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