WORLD ORGANISATION FOR ANIMAL HEALTH
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AD HOC GROUP ON HIGH THROUGHPUT SEQUENCING, BIOINFORMATICS AND COMPUTATIONAL GENOMICS (HTS-BCG) [1]

Paris, 13–14 November 2014

An *ad hoc* Group (AHG) on High Throughput Sequencing, Bioinformatics and Computational Genomics (HTS-BCG) was convened at the OIE Headquarters from 13 to 14 November 2014.

The Agenda and List of Participants are given at Appendices I and II, respectively.

1. Opening

Dr Elisabeth Erlacher-Vindel, Deputy Head of the Scientific and Technical Department, welcomed the participants of the meeting on behalf of Dr Bernard Vallat, Director General of the OIE. She explained that the specific task of the Group was to develop an OIE strategy on the topic to be used ultimately by the OIE, the OIE Reference Laboratory and Collaborating Centre (Reference Centre) network and the OIE Member Countries.

2. Appointment of chairperson and rapporteur

The meeting was chaired by Prof. Massimo Palmarini, and Dr Peter Daniels was designated as rapporteur.

3. Terms of Reference for the *ad hoc* Group meeting

The Terms of Reference (ToRs) were adopted with minor modifications; they can be found at Appendix III.

The AHG discussed the challenges presented by the increasing utilisation of HTS-BCG in pathogen discovery and characterisation, and the subsequent interpretation of results in respect of clinical disease manifestation, and validity of diagnostic tools and vaccines. The Group acknowledged that HTS-BCG was a rapidly developing technology mostly driven by available platforms and software packages for sequence generation, with few standards for quality assurance of the results. Different to other diagnostic technologies, the Group recognised both the need for and the opportunity to develop standards regarding the generation of sequence information.

Leadership was necessary in assessing the implications of the technology for animal health, international trade and disease status and control, and the OIE was considered the appropriate organisation to provide this leadership. The recent discovery, characterisation and assessment of the animal health implications of the Schmallenberg virus were considered a good example of the opportunities and challenges related to the use of HTS-BCG. The Group considered it likely that the number of such discoveries would become more frequent with time. It identified the need for a regular permanent monitoring mechanism and the establishment of a regular permanent process for the assessment of the implications of the findings for animal health, trade and disease status and control.

[1] Note: This ad hoc Group report reflects the views of its members and may not necessarily reflect the views of the OIE. This report should be read in conjunction with the January 2015 report of the Biological Standards Commission because this report provides its considerations and comments. It is available at: http://www.oie.int/en/international-standard-setting/specialists-commissions-groups/laboratories-commission-reports/meetings-reports/

Due to the sensitivity of the technology for detecting genetic material, maintenance of the genetic integrity of specimen and samples is of paramount importance. Whilst there was guidance for the different commercially available sequencing platforms and kits, the Group noted the need for general guidance and standards on critical aspects of HTS-BCG. In a future step, the OIE would need to consider disease-specific implications of the technology.

In consideration of the Terms of Reference for this meeting, the Group agreed that both charges would need to be advanced in parallel.

3.1. To further elaborate the concept for the Pilot Project: *Creation of an OIE platform for the collection and management of genomic sequences in animal health*

The Group discussed the state of affairs subsequent to the Third Global Conference of OIE Reference Centres (14–16 October 2014, Incheon, Korea [Rep. of]).

It was noted that the OIE continually adapts to animal health challenges, such as changing emphasis from focusing on diseases to developing standards for dealing with infections. Responding to the challenge of managing sequence information is part of this continuum. Genetic sequences for infectious agents, including for animal pathogens relevant to the work of the OIE, would likely be generated in even greater numbers in the future. This could potentially have implications for international trade and disease management. It was therefore considered necessary for the OIE to prepare a recording system that would allow capture and access to genetic sequence information stemming from relevant animal health alerts.

Such a system should (a) consider the need for reference genetic sequences and pathogens (biological references), (b) accommodate the fact that pathogens are likely to evolve and change over time, so that new or modified references would need to be added over time, (c) address the phenotypic implication of genetic sequence information, such as differences in clinical signs or the need to adapt vaccines and diagnostics, and (d) enable the OIE to address trade implications and disease control implications for diseases of concern to the OIE.

Importantly, the OIE system should be capable of and routinely decide on the significance of descriptions of new infectious agents, including those based solely on the reporting of novel sequences or new variations of previously recognised genetic profiles. This will involve a monitoring capacity to flag new pathogens or strains, a rapid and regular mechanism for evaluation of the new information and a process of consultation to advise on implications for trade, disease status and disease control.

The Group extensively discussed the idea of the pilot project. It agreed that the OIE platform should hold sequence data combined with relevant epidemiological information. The Group considered the project as needing full time personnel guided by Professor Caporale as the project coordinator representing the OIE to advance in a reasonable time frame that is matched to advances in the technology and international efforts to drive standardisation. The Group recognised the expertise already available amongst the OIE Reference Centres and the need for acceptance of the project.

3.2. To develop standards for high throughput sequencing, bioinformatics and computational genomics for inclusion in the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals*

The Group agreed that it would be worth developing specific standards for HTS-BCG for inclusion in the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* (*Terrestrial Manual*) to give guidance to potential users of the technology for purposes relevant to animal health. Due to the nature of the methodology, there is potential for it to be used outside the context of quality assured laboratories, and there are potentially far-reaching implications, which set this methodology apart from other diagnostic methodologies.

A first draft of a potential chapter based on the report of the first meeting of the AHG was reviewed. The Group agreed that the methodology would always be used as a primary diagnostic tool, whether the specific purpose was pathogen discovery or confirmation of the genetic sequence of a suspected or known pathogen. Additional guidance was developed to address procedural differences in approach for these two use scenarios.

Maintaining the integrity of the genetic information contained in the original sample was a key challenge of the methodology and further recommendations to ensure genetic integrity were developed.

A generic guide to the key steps involved in HTS-BCG was developed for a public interested in taking up the technology in an animal health related context.

The Group further developed a new section on interpretation of results, stressing the importance of the relevant context of the interpretation of results, including appropriate preparation of genetic reference libraries, the epidemiological context, and the use of reference sequences, where available.

The draft chapter can be found at Appendix IV of this report. The draft Chapter will be submitted to the Biological Standards Commission for review and forwarding to Member Countries for comment.

3.3. Draft Work Plan

The Group agreed that two work plans would be required that needed to progress in parallel. One needed to advance the OIE pilot project, the other should consider the development of OIE standards.

Regarding the concept for the Pilot Project: Creation of an OIE platform for the collection and management of genomic sequences in animal health, the need to have staff fully dedicated to this project was recognised and the following steps for the Pilot Project were proposed:

1. Conduct a process of consultation with selected OIE Reference Centres to more fully develop the functional specifications to implement a pilot project based on the proposed platform framework and on country/laboratory visits.
2. Understanding of current systems used in the scientific community would be sought through a questionnaire.
3. Based on consideration of experience and solutions available from the OIE Reference Centres, develop the draft functional specifications for an OIE platform solution for managing sequence data and accompanying epidemiological information, ensuring interoperability with WAHIS[2].
4. Develop acceptance of the functional specifications through a process of iteration with the OIE Reference Centres leading to a pilot entry of data to the platform. Bluetongue is recommended for this pilot data entry.
5. In a second phase, progress to other diseases is envisaged (foot and mouth disease [FMD], avian influenza, Newcastle disease, etc.).
6. Upon successful completion of these two phases and presentation to the Member Countries, the system could be launched.

Regarding the development of OIE standards, the Group recommended the following steps:

1. The adoption of a draft chapter on general aspects of HTS-BCG for inclusion in the *Terrestrial Manual* as the first step.
2. Reconvene the *ad hoc* Group with additional expertise to consider:
    a. horizontal issues of the technology, such as appropriate validation of the technology;
    b. specific requirements for quality assurance;
    c. bioinformatics;
    d. disease-specific implications of the technology.

[2] WAHIS: World Animal Health Information System (of the OIE)

All work will be progressed taking into account the responses to the OIE questionnaire on the use of the technology that was sent out to the Reference Centres in preparation of the Third Global Conference of OIE Reference Centres.

4. Provide input on the programme for the 1-day OIE Seminar on *New Diagnostic Technologies and International Standard Stetting* to be held on Wednesday 17 June 2015 in Saskatoon, Canada during the WAVLD[3] Symposium

The Group considered the title of the meeting in the light of the discussions around the draft *Terrestrial Manual* chapter and the proposed OIE Pilot Project *Creation of an OIE platform for the collection and management of genomic sequences in animal health.* It suggested that the seminar would use whole genome sequencing as an example diagnostic method and the discussions be structured around the sections of the draft *Terrestrial Manual* chapter on HTS-BCG.

The following topics were suggested:

- OIE introduction
- HTS-BCG: Evolution or revolution?
- The increasing importance of sequence information in managing animal health information globally; actions by the OIE in response to the increasing detection of new agents and new variants described by sequence information
- Approaches to validation of HTS in the diagnostic laboratory
- Bioinformatics (how to standardise) / assembling raw data into sequences. What does it mean for a lab to use such technologies (example?)
- New types of bluetongue –animal health issues arising from reports of different sequences of known viruses
- Quality assurance of HTS in the diagnostic laboratory
- Genetic evolution of avian influenza in Asia and related challenges
- Data interpretation
- Opportunity given by this technology to study the spread of diseases in time and space (*animated maps*)

5. Any other matters

The Chair reported on his consultations with FAO[4] regarding the sharing of FMD sequences among the scientific community linked to geographical information. He had informed the FAO of the OIE pilot project and noted the potential for overlap between the two projects.

6. Finalisation and adoption of the draft report

The AHG finalised and adopted the draft report.

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…/Appendices

[3] WAVLD: World Association of Veterinary Laboratory Diagnosticians

[4] FAO: Food and Agriculture Organization of the United Nations

Appendix I

AD HOC BRAINSTORMING GROUP ON HIGH THROUGHPUT SEQUENCING, BIOINFORMATICS AND COMPUTATIONAL GENOMICS (HTS-BCG)

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Agenda

1. Opening
2. Appointment of chairperson and rapporteur
3. Terms of Reference for the *ad hoc* Group meeting
   - 3.1. To further elaborate the concept for the Pilot Project: *Creation of an OIE platform for the collection and management of genomic sequences in animal health*
   - 3.2. To develop standards for high throughput sequencing, bioinformatics and computational genomics for inclusion in the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals*
   - 3.3. Draft Work Plan
4. Provide input on the programme for the 1-day OIE Seminar on *New Diagnostic Technologies and International Standard Stetting* to be held on Wednesday 17 June 2015 in Saskatoon, Canada during the WAVLD[5] Symposium
5. Any other matters
6. Finalisation and adoption of the draft report

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[5] WAVLD: World Association of Veterinary Laboratory Diagnosticians

Appendix II

AD HOC BRAINSTORMING GROUP ON HIGH THROUGHPUT SEQUENCING, BIOINFORMATICS AND COMPUTATIONAL GENOMICS (HTS-BCG)

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Appendix III

AD HOC BRAINSTORMING GROUP ON HIGH THROUGHPUT SEQUENCING, BIOINFORMATICS AND COMPUTATIONAL GENOMICS (HTS-BCG)

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Terms of Reference

1. To further elaborate the concept for the Pilot Project: *Creation of an OIE platform for the collection and management of genomic sequences in animal health*

2. To develop standards for high throughput sequencing, bioinformatics and computational genomics for inclusion in the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals*

3. Draft Work Plan

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