



**AD HOC GROUP ON HIGH THROUGHPUT SEQUENCING,  
BIOINFORMATICS AND COMPUTATIONAL GENOMICS (HTS-BCG)<sup>1</sup>**

**Paris, 7–9 December 2015**

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The Third meeting of the OIE *ad hoc* Group (AHG) on High Throughput Sequencing, Bioinformatics and Computational Genomics (HTS-BCG) was convened at the OIE Headquarters from 7 to 9 December 2015.

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 on behalf of Dr Bernard Vallat, Director General of the OIE, and of Dr Monique Eloit, Director General elect who would begin her 5-year term of office in January 2016. Dr Erlacher-Vindel explained that the specific task of the Group was to develop a clear and detailed plan on how the OIE Platform Project could be implemented: *Creation of an OIE platform for the collection and management of genomic sequences in animal health* to complement the epidemiological database within WAHIS<sup>2</sup>.

**2. Appointment of chairperson and rapporteur**

The meeting was chaired by Prof. Massimo Palmarini, and Dr Antonino Caminiti was designated as rapporteur.

**3. Update on actions taken since the last *ad hoc* Group meeting**

At its last meeting in November 2014, 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. To this end an introductory chapter entitled *Standards for high throughput sequencing, bioinformatics and computational genomics* had been drafted and sent to OIE Member Countries in October 2015 for first-round comment. If the chapter is well received it could be proposed for adoption by the Assembly in May 2016.

The Group had also previously provided input on the programme for the 1-day OIE Seminar on *New Diagnostic Technologies and International Standard Setting* that was held on 17 June 2015 in Saskatoon, Canada during the WAVLD<sup>3</sup> Symposium. The eleven presentations highlighted a spectrum of new tools, including HTS-BCG, along with their potential problems and challenges. These new technologies become even more robust when linked to epidemiological information. Participants found the seminar to be interesting, practical, timely and of scientific importance. The PowerPoint presentations and abstracts of the OIE seminar are available on the OIE Website at: <http://www.oie.int/eng/WAVLD2015/presentations.htm>.

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<sup>1</sup> 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 February 2016 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/>

<sup>2</sup> WAHIS: World Animal Health Information System

<sup>3</sup> WAVLD: World Association of Veterinary Laboratory Diagnosticians

#### **4. Review draft work plan and assess what has been done and what steps are needed for implementation of the platform project**

The Group took note of Recommendation 2 of Resolution No. 33, adopted by the OIE World Assembly in May 2015, which states: “The OIE establish a platform for the collection and management of partial and complete genomic sequences (including genotype assignment) with the aim to integrate the reporting of genomic sequence data into the OIE World Animal Health Information System (WAHIS), with the collective support of OIE Reference Centres, and involving all OIE Member Countries.”

In accordance with this recommendation, the Group proposed that the initial model for the OIE platform be the creation of a centralised rather than a decentralised system.

The purpose of the OIE sequence database maintained within WAHIS is to provide a permanent and official record of the genetic sequences (preferably whole genome sequences) of the pathogens/infectious agents that have been the subject of Member Country reports to WAHIS, whether immediate notification or 6-monthly reports. (NB. The purpose of the OIE sequence database is NOT to be a full and complete record of the sequences of infectious agents detected in animal populations, but rather the record of the pathogens/infectious agents involved in animal health events reported by Member Countries.)

The Group suggested that the priority for the OIE be to establish this genomic platform managed by the OIE itself. The establishment of linked institutional databases and broader pathogen-specific databases connected to the platform would be a desirable objective to be left for a later stage once the platform has been established. These would require the full involvement of OIE Reference Centres and other communities of experts.

Modules with analysis tools will also be useful but are not essential for the initial stage of the project. However, modules to facilitate the upload of curated sequences at the local level might need to be considered within this project and will have to be considered for the implementation stage.

This approach best fulfils Resolution No. 33 and would also result in a focused and feasible project.

#### **5. Assess the pilot project and detail the steps needed for implementation**

Based on the Terms of Reference, the Group determined that the OIE platform project has two main goals:

1. Establishment of a pathogen genomic platform
  - a) Refine the vision for the platform;
  - b) Suggest next steps for its implementation.
2. Definition of standards to be used for the sequence information to be uploaded in the platform.

The Group agreed that the principal output of this meeting would be a revision of the draft pilot project. This document (see [Appendix III](#)) details the objectives, strategy and architecture of the OIE platform. The second output would be consensus comments on the draft *Terrestrial Manual* chapter. These comments, together with those submitted by OIE Member Countries, would be considered by the OIE Biological Standards Commission (BSC).

The practical recommendations for the establishment of the genomic platform are the following:

1. The appointment of a full-time Project Manager to work within the framework of the next version of WAHIS. The role of the Project Manager is to define the technical specifications of the genomic platform, including the system connectivity in the first instance. The Project Manager should be based at the OIE Headquarters working in close collaboration with the Information, Administration, Logistics and Publications Dept, World Animal Health Information and Analysis Dept and the Scientific and Technical Dept.

2. The *ad hoc* Group could provide guidance and support to the Project Manager and meet on a regular basis to follow up the project implementation. This would ensure close links with the BSC and transparency for the Member Countries.
3. Once the technical specifications of the project have been finalised, it should be put to tender within the WAHIS project.

Members of the Group discussed the draft *Terrestrial Manual* chapter and helped to identify steps in the process that were not yet fully covered in the text. The Group made appropriate recommendations, which will be considered in the process of overall review of the chapter. These included the necessity to clearly identify the purpose of the application of the technology, the appropriateness of the specimens for that purpose and the corresponding preparations of the samples for testing and the preparation and quality control of sequence data. A consolidated version of the chapter will be forwarded to the BSC for consideration along with Member Country comments.

## **6. Any other matters**

None

## **7. Finalisation and adoption of the draft report**

The AHG finalised and adopted the draft report.

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.../Appendices

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**Agenda**

1. Opening
  2. Appointment of chairperson and rapporteur
  3. Update on actions taken since the last *ad hoc* Group meeting
  4. Review draft work plan and assess what has been done and what steps are needed for implementation of the platform project
  5. Assess the pilot project and detail the steps needed for implementation
  6. Any other matters
  7. Finalisation and adoption of the draft report
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BIOINFORMATICS AND COMPUTATIONAL GENOMICS (HTS-BCG)**

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**Terms of Reference**

1. Review draft work plan and assess what has been done and what steps are needed for implementation
  2. Assess the pilot project and detail the steps needed for implementation
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## OIE PATHOGEN GENOMICS PLATFORM

### CREATION OF AN OIE PLATFORM FOR THE COLLECTION AND MANAGEMENT OF GENOMIC SEQUENCES IN ANIMAL HEALTH

#### 1. INTRODUCTION

The use of high throughput sequencing (HTS), bioinformatics, computational genomics (BCG) and metagenomics in the veterinary field is increasing. Sequence information is, therefore, increasingly playing a role in the diagnosis and management of microbial infections, in the characterisation of infectious agents, and the traceability of their spread over time.

The growing reliance on generating and using sequence information and the concurrent ever-increasing trend toward global open information systems will have crucial and far-reaching implications for veterinary laboratories, including the traditional notification and management of infectious diseases and food-borne infections.

The OIE has a leading and central role in the management, interpretation and use of information in animal health. The OIE also develops standards for the generation of data during investigations of animal infections on the farm and at any point along the “value chain” linking animals to consumers.

The OIE considers that pathogen genomic sequences and the associated sequence analysis data should be an integral and necessary part of the reporting of cases and outbreaks of disease at the international level. New technological tools, including HTS-BCG and metagenomics, should therefore be introduced and used in the context of accepted practices in animal disease diagnostic and control processes, including laboratory quality assurance systems.

Sequence data, in particular those referring to whole pathogen genomes, are very relevant not only in the epidemiological context but also in improving the understanding of disease pathogenesis and host responses. It can thus be envisaged that sequence databases of major veterinary pathogens will have an ever-increasing role in animal health especially if enriched by related metadata.

Strategies, policies and practices for analysing and managing genomic sequences and related metadata are, therefore, a priority on the OIE agenda. The primary objective is to develop a comprehensive approach and an *open access* database within the OIE World Animal Health Information System (WAHIS) to collect, store and share sequence information relating to animal disease events and their control. Additionally, it will be necessary to develop standards for the generation, storage, management and interpretation of sequences and their related epidemiological data.

The OIE intends to make full use of the competence and expertise of its worldwide Reference Centre network in the development of policies and practices for the management and use of sequence information. To this end, the OIE is developing standards for the management of HTS-BCG for inclusion in the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (Terrestrial Manual)*. In the future, sequence data will be included in WAHIS and the OIE Reference Centre network will play a key role in this project.

#### 2. DEFINITION OF THE OIE STRATEGY

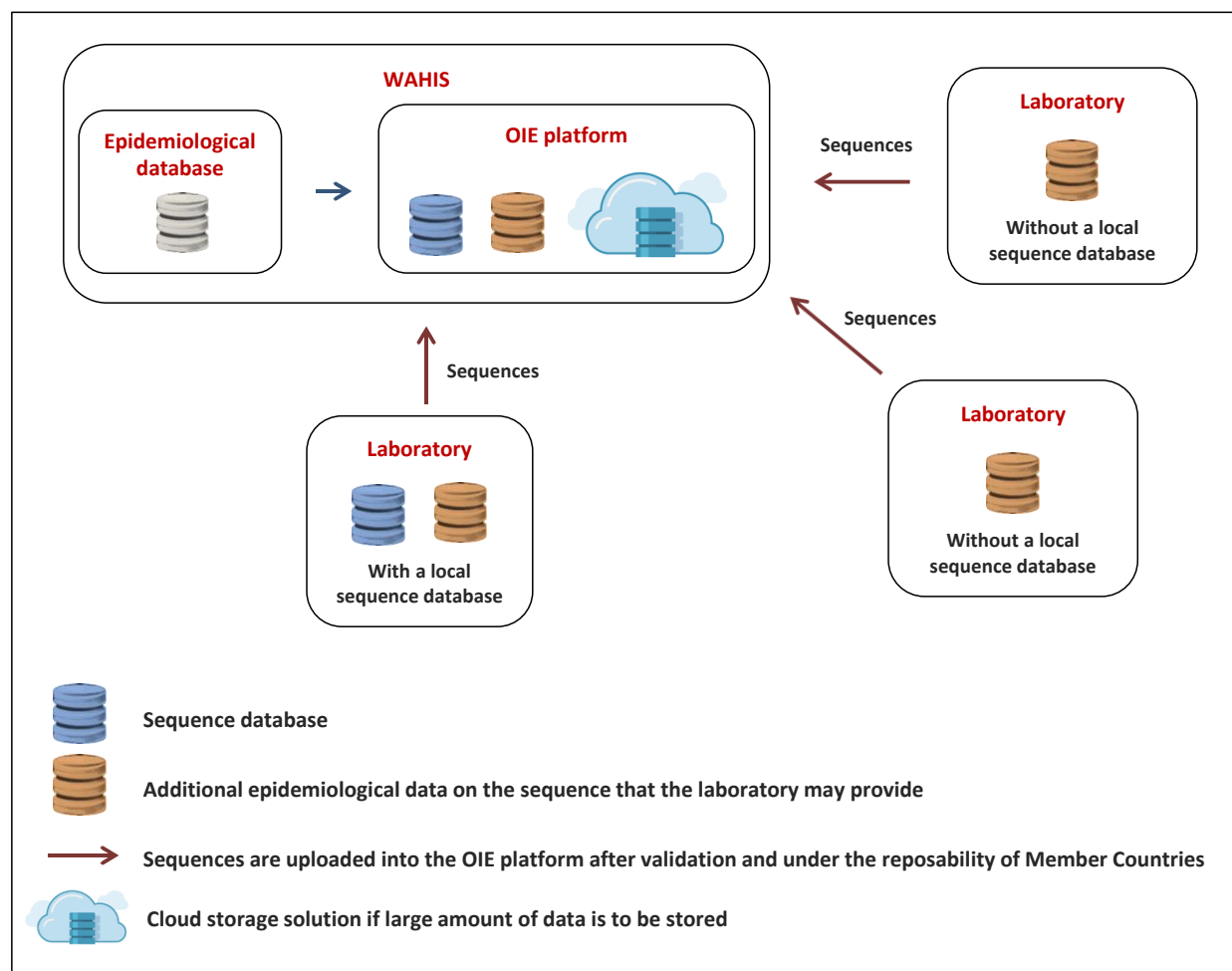
The strategy of the OIE is to provide a permanent and official record of the genetic sequences (preferably whole genome sequences) of pathogens that have been the subject of country reports to the OIE (whether immediate notifications or 6-monthly reports). The OIE does not intend to provide a sequence database to be a full and complete record of the sequences of infectious agents detected in animal populations, but rather to provide a record of the pathogens/infectious agents involved in animal health events reported to the OIE by Member Countries.

The sequence information should be stored within WAHIS, which would then include two components: (i) the epidemiological database and (ii) the OIE pathogen genomics platform (hereafter referred to as the OIE platform). Each sequence will be systematically linked to the corresponding epidemiological information within WAHIS.

The overall strategy should include a process of defining standards for production, assembly and storage of genomic sequences to be integrated into the OIE *Terrestrial Manual* and the OIE *Manual of Diagnostic Tests for Aquatic Animals (Aquatic Manual)*.

### 3. OVERVIEW OF THE OIE PLATFORM

The OIE platform will provide an open and transparent centralised system with the OIE Reference Laboratories or national reference laboratories generating and providing the genetic sequence information (hub–spoke model) under the responsibility of the OIE Delegate (Figure 1).



**Figure 1. Overview of the OIE platform.**

According to this model, laboratories may or may not host local databases and may or may not have the infrastructure to upload sequences to the OIE platform. Consequently, the OIE will provide web interfaces to upload sequences to the OIE platform, which is intended to be flexible and allow sequence submission in several ways.

WAHIS will link the epidemiological data with the corresponding pathogen sequences. However, from a structural point of view, the epidemiological database and the OIE platform will be separated to add flexibility to the overall system.

Member Countries will be responsible for the sequence submission to the OIE platform.

In compliance with the objective of the OIE to ensure transparency in animal health and the open access nature of data stored in WAHIS, sequence data stored in the OIE platform should be equally accessible.



The adoption of this model for the OIE platform does not preclude:

- i) the establishment of separated local databases or pathogen-based databases maintained by the OIE Reference Centres. Indeed, the OIE encourages OIE Reference Centres to engage in networking activities and this would equally apply to such databases;
- ii) the possibility that the OIE platform could provide services of different nature in the future (e.g. modules for data analysis provided by OIE Reference Centres or links to other resources of the OIE network).

The system design should be stable and robust but adaptable to evolving methodologies and technologies.

#### 4. ARCHITECTURE OF THE OIE PLATFORM

The structure of the OIE platform (Figure 2) will consist of the following components:

- i) Genomic sequence database linked, but structurally separated, to the epidemiological component of WAHIS;
- ii) Interface module for uploading the sequence data;
- iii) Connection module to link the genomic sequences to the corresponding epidemiological data stored in WAHIS;
- iv) Administration module for data management, user access control and data workflow.

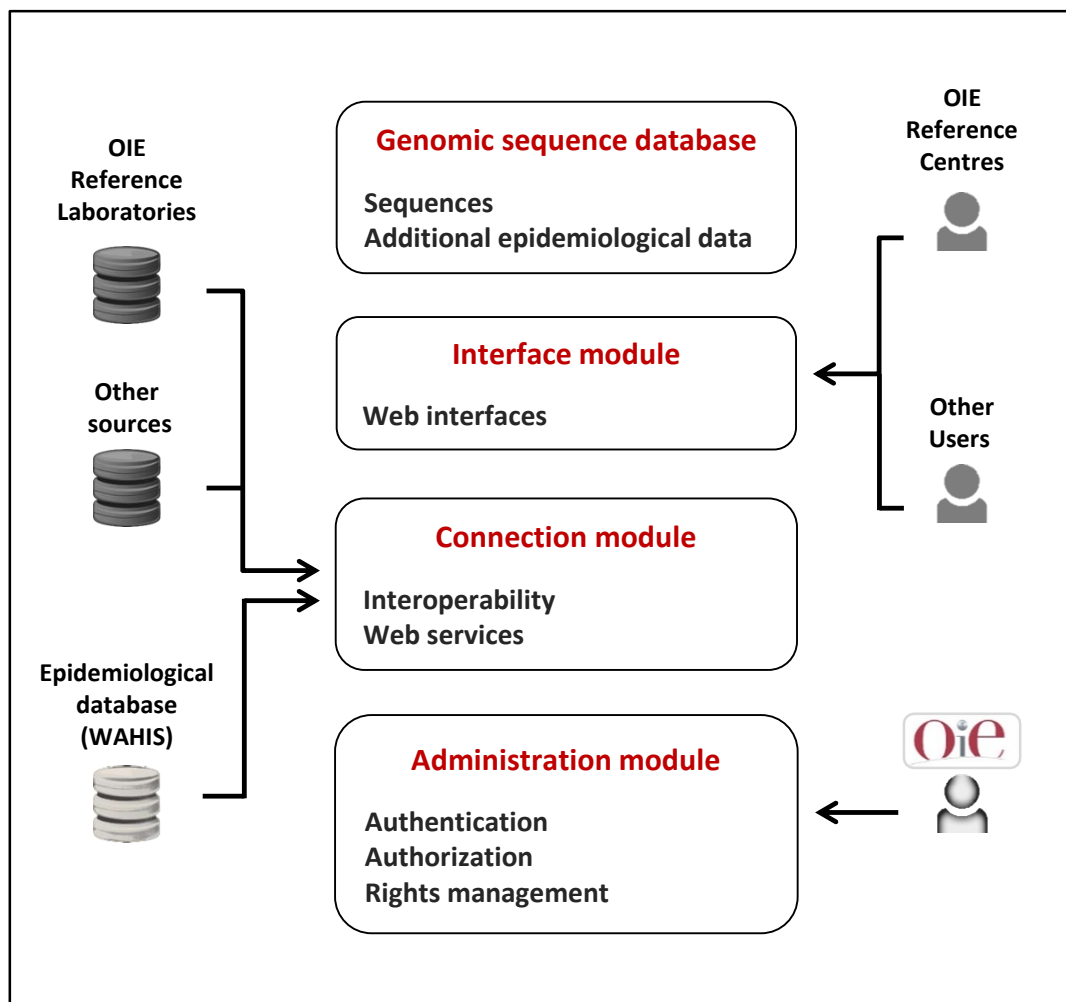


Figure 2. Architecture of the OIE platform.

## 5. COMPONENTS

### 5.1. Genomic sequence database

The genomic sequence database is the core component of the OIE platform. This database will allow genomic sequences to be stored, indexed, searched and available.

The database must support the complex and evolving set of data associated with the sequence and the sequence information itself. Sequence files are most naturally stored in a flat file format.

For each genomic sequence, the database will collect and store metadata on the technology and methodology used to generate the sequence data, and any additional epidemiological data that the submitting laboratory may decide to provide.

Data should be collected and stored in accordance with the standards outlined in chapter 1.1.11 of the *Terrestrial Manual* entitled *Standards for high throughput sequencing, bioinformatics and computational genomics*.

### 5.2. Interface module

The interface module will enable the laboratory to upload sequence data. Two prerequisites to upload a sequence to the platform are i) the creation of a link between the platform and the WAHIS, and ii) the meeting of standards set out by the OIE.

### 5.3. Connection module

The connection module is an interoperability module that assures the connectivity between the genomic sequence database with the epidemiological data stored in WAHIS.

### 5.4. Administration module

Similarly to the epidemiological component of WAHIS, the OIE platform will collect and store potentially sensitive information. This poses security challenges for the OIE platform. For this reason, it is important to implement an administration module and appropriate standards to manage the data at different levels and for different activities such as the uploading and access of the genomic sequences.

This module will guarantee compliance with quality requirements outlined in chapter 1.1.11 of the *Terrestrial Manual* during the uploading of the sequences, it will manage visibility and access of data, and it will trace information on the use of data. Issues surrounding intellectual property rights need to be addressed by the OIE and a common policy needs to be agreed.

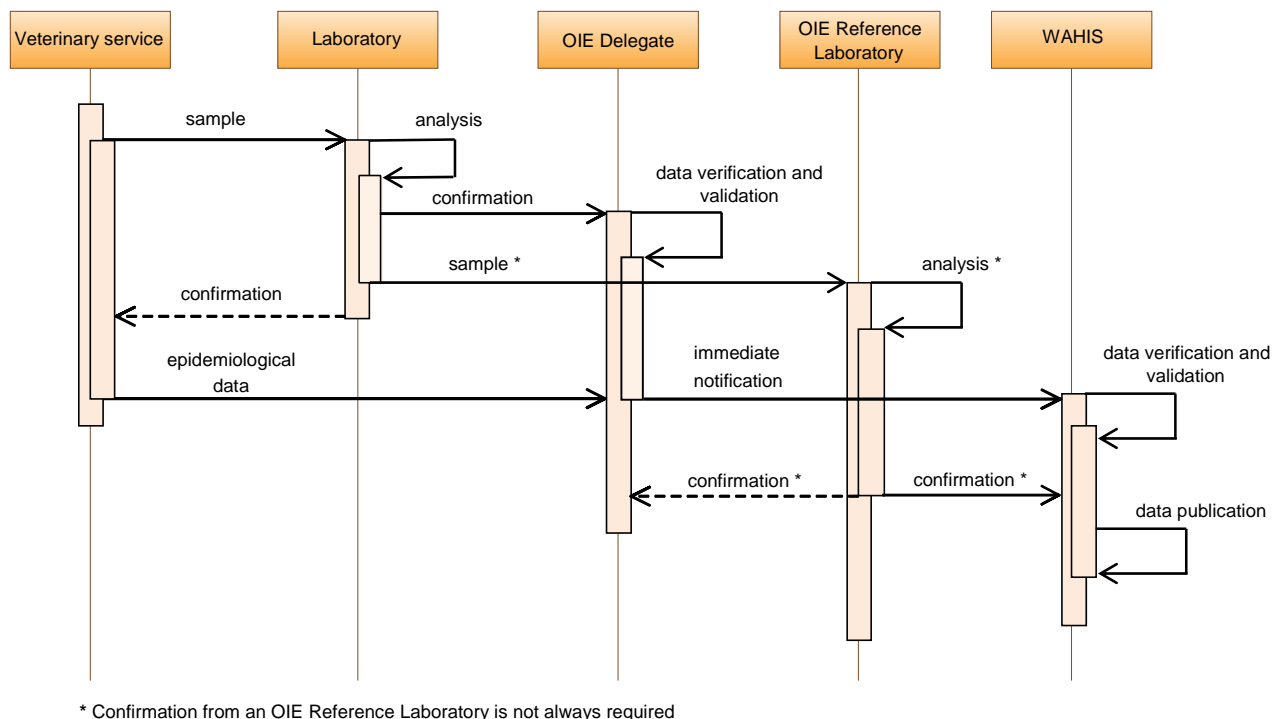
Because the amount of sequence information will increase over time, the OIE platform must be extensible.

## 6. DATA FLOWS

The OIE requires that Member Countries notify any event of epidemiological significance (immediate notifications and follow-ups) and transmit periodic reports on the presence or absence of OIE listed diseases (6-monthly reports). Official communications between Member Countries and the OIE are subject to strict procedures, and the publication of data follows a series of steps before information is made public.

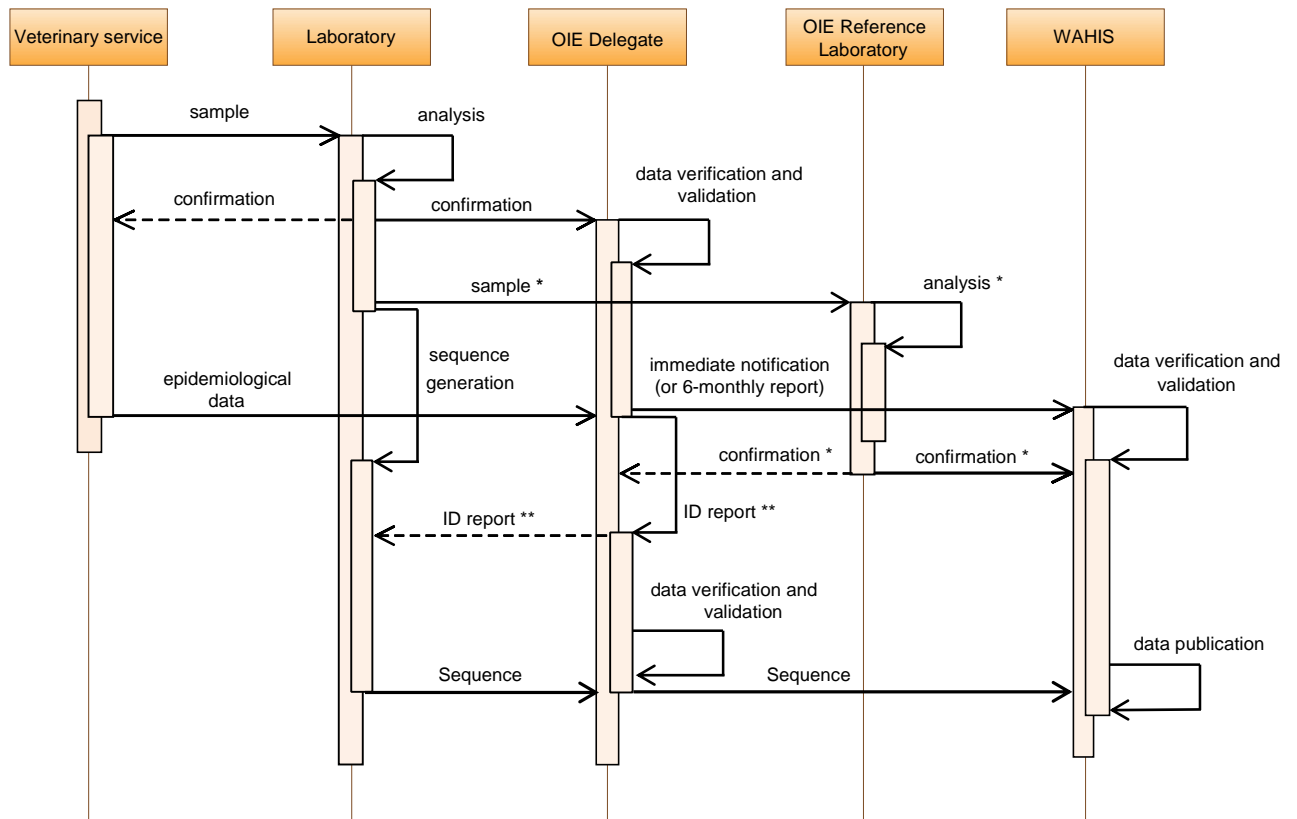
Figure 3 shows the current data flow of an immediate notification.

Following an immediate notification, OIE Member Countries will be required to upload to the platform the sequences of pathogens isolated in the outbreak (or in the group of outbreaks) reported in that notification. The requirement to provide sequence information should not delay the initial immediate reporting.



**Figure 3. Current data flow of an immediate notification to OIE.**

Figure 4 shows the possible data flow for the upload of the sequences following an immediate notification or related to the 6-monthly report. The sequence information should be transmitted through the OIE platform and linked to the corresponding epidemiological data in WAHIS (in the diagram, the box WAHIS includes the new OIE platform).



\* Confirmation from an OIE Reference Laboratory is not always required

\*\* Or any other way to establish a link between the sequence and the corresponding epidemiological data stored in WAHIS

**Figure 4. Suggested data flow in the proposed system for the upload of pathogen genomic sequences following an immediate notification (or related to a 6-monthly report)**