




OIE/FAO Network of Expertise on Avian Influenza

# OFFLU activities at the Human-Animal interface

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Steve Edwards - *chairman*

Food and Agriculture Organization of the United Nations  
Animal Production and Health Division






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# OIE/FAO Animal Influenza Network (OFFLU)

- Created in April 2005
- [www.offlu.net](http://www.offlu.net)

Food and Agriculture Organization of the United Nations  
Animal Production and Health Division

OIE/FAO Network of Expertise on Avian Influenza

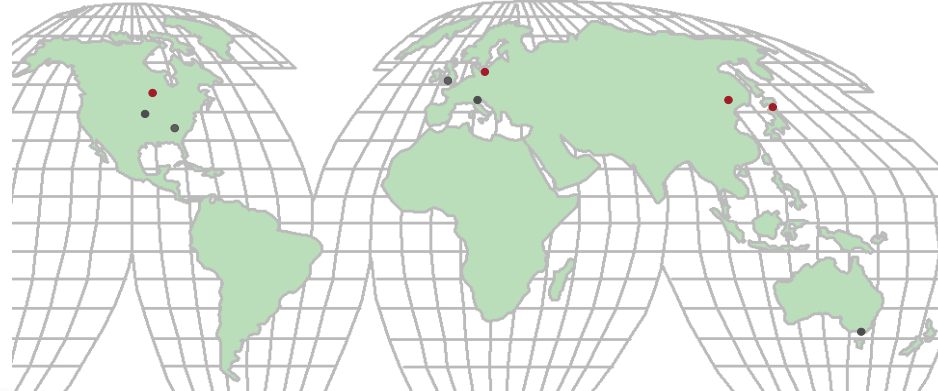
## OFFLU objectives

- exchange scientific data and biological materials
- offer technical advice and veterinary expertise to member countries
- collaborate with the WHO influenza network
- support avian influenza research

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### OIE Reference Laboratories and FAO Reference Centres for Avian Influenza and Newcastle Disease



- OIE Reference Laboratory (or Collaborating Centre in the case of SEPRL -USA) and FAO Reference Centre
- OIE Reference Laboratory

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## Main on-going OFFLU achievements

- **Active collection of strains.** Bridge between the field, FAO/EU/other funded projects and the scientific community, including medical virologists.




– OIE Resolution - *Sharing of avian influenza viral material and information in support of global avian influenza prevention and control*

### RESOLUTION No. XXVI

#### Sharing of avian influenza viral material and information in support of global avian influenza prevention and control

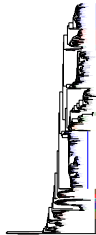
Endorsed by 172 OIE country members

1. OIE Members reporting outbreaks of avian influenza **should agree to share animal avian influenza viral material and information about avian influenza viruses through OFFLU** with the international scientific community.
2. OIE Reference Laboratories must actively encourage sharing of material and data with the international scientific community, and as a **minimum deposit genetic data within 3 months of receiving an isolate** into a public database designated by the OFFLU Steering Committee, which will manage scientific relations with the WHO.
3. To enhance cooperation and transparency, the actions taken by countries must be recognised in subsequent publications and other benefits arising from the use of biological material or data that they have submitted to OIE Reference Laboratories.

OFFLU MTA		Animal Health Service AGAH
 <p><b>MATERIAL TRANSFER AGREEMENT</b></p> <p>This Material Transfer Agreement is made this _____ day of _____, by and between,</p> <p><b>Provider:</b> .....</p> <p>and</p> <p><b>Recipient:</b> .....</p> <p>The parties have agreed as follows:</p> <ol style="list-style-type: none"> <li>Provider agrees to transfer to Recipient the following (biological) material: H5N1 avian influenza virus isolates, as described in more detail in Annex 1 (hereinafter "Material").</li> <li>The shipper will be responsible for the appropriate preparation of the parcel according to IATA' standards and for identifying a shipping company with the appropriate authorization to handle infectious material (Code UN2814). The parcel will be delivered through (name of the shipping company/other mechanism).</li> <li>This Material will be used by Recipient solely for research purposes in connection with the project titled (name of the related project, if any): Specific activities to be undertaken under the project are: - Activity 1; - Activity 2. (hereinafter referred to as "Project")</li> <li>By requesting the material and signing this agreement, the recipient accepts responsibility for the proper handling and testing of the Material in accordance with generally accepted international scientific standards, such as the relevant WHO and OIE guidelines and standards related to avian influenza. The Recipient guarantees that suitable handling and containment conditions are available and will be applied in the Recipient's laboratory.</li> <li>The Material will not be used for commercial purposes, such as production or sale of products or services, for which a commercialization licence may be required. The</li> </ol>	<p>Project, inform Provider of the results of the</p> <p>shall, or may be construed as, granting all for any use other than for purposes of ment. The Provider exclusively reserves, including patentable information and for this Agreement, including, without any ate, sell or distribute, privately or publicly,</p> <p>ic or publish in any form any information, tion of a strategic or commercial nature, uthorized in writing by the Provider. The s, to private or company advantage. This ination of this Agreement.</p> <p>Recipient shall retain control over this of the Material to other people not under approval of the Provider. The Provider to third parties or use the Material for its</p> <p>ent with no warranties, expressed or implied, nness for a particular purpose. The Provider he Material will not infringe any patent or er shall have no liability to the Recipient for al by the Recipient under this agreement.</p> <p>Listed infectious disease agents" that were tal sent.</p> <p>.OFFLU secretariat for its records.</p> <p>stributed in accordance with the laws of United ection with this Agreement shall be settled in of Recipient country.</p> <p><b>PROVIDER</b> Place: _____ Date: _____ By: _____ Title: _____ By: _____ Title: _____</p> <p>1/11</p>	<p>ANNEX 1</p> <p>THE MATERIAL TRANSFERED</p> <p>(scientific names, quantity, units of materials etc)</p>

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<h2>Main on-going OFFLU achievements</h2> 	
<ul style="list-style-type: none"> <li>• Active collection of strains</li> <li>• <b>7 OFFLU technical groups:</b> <ul style="list-style-type: none"> <li>– commercial kits evaluation, applied epidemiology, biosafety, vaccination, proficiency testing, human-animal interface, common standards sera/RNA</li> </ul> </li> </ul>	
	
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## Main on-going OFFLU achievements



- Active collection of strains
- 7 OFFLU technical groups
- Contribution to establishment of a **Unified Nomenclature System for H5N1 influenza viruses based on HA gene phylogeny** (WHO/FAO/OIE, 2007)



## Main on-going OFFLU achievements



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- **Evaluation of a new publicly accessible platform (EpiFluDB) in link with WHO**



# GISAID/EpiFluDB



As of 7 Oct 08:

3,475 isolates (avian and human) submitted  
 + 18,508 isolates uploaded from Genbank  
 = 21,983 isolates (72,848 sequences)

- **Organization** of the data at the isolate level, instead of the segment
- **Curation** of existing sequences
- **Searchability** of most of the data fields

*i.e. type, H/N-types, host, location, collection/submission dates, min. sequence length, isolate name, passage history, ID, sequence submitter lab*

# GISAID/EpiFluDB



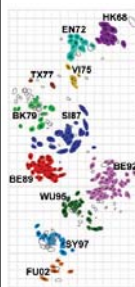
## EpiFluDB Development 2008-2010

2008	2009	2010
EpiFluDB specification and development Alpha version – January 2008	Training of scientists to the use of EpiFluDB (year long / users meeting / key influenza conferences)	Training of scientists to the use of EpiFluDB (year long / users meeting / key influenza conferences)
EpiFluDB browsing and single data upload Mechanism – February 2008	Extension of the user base (>200 scientists)	Extension of the user base (>500 scientists)
EpiFluDB evaluation and improvement plan Early May 2008	Improvement and additional bioinformatic tools Global phylogeny analysis "grant submission"	Fail-over for EpiFluDB established at A remote site (in Switzerland), allowing 24/7 Accessibility (Basel / Zuerich ?)
EpiFluDB « alive » May 2008	Installation of the computing power for EpiFluDB	Continued development and improvement of The EpiFluDB according to community Feedback (1 FTE for maintenance/ 2 for Development stages)
Data deposition for vaccines selection August 2008	Collaborative effort for implementing guidelines in influenza Community (human and avian), EpiFluDB role as a facilitator	
Evaluation and development suggestions from OFFLU network (FAO-OIE) Mid-August 2008	Description distribution of the annotation procedure for viral gene sequences at protein level	
Annotation procedures/ improvements October 2008	EpiFluDB part of European and US grant submission (for the next 3 years financing)	
Bioinformatics annotation tools resistance computation antigenic cartography	Publication of EpiFluDB for an NAR Database issue (deadline Jun 2009)	
External databases linking		

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## Main on-going OFFLU achievements



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- Contribution to establishment of a Unified Nomenclature System for H5N1 influenza viruses based on HA gene phylogeny (WHO/FAO/OIE, 2007)
- Evaluation of a new publicly accessible platform (EpiFluDB) in link with WHO
- **OFFLU projects on vaccination in Indonesia and Egypt** (Implemented by FAO)



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## OFFLU national projects in Indonesia and Egypt

Purpose:

### Assessment of vaccine efficacy

- virus characterization
- challenge tests
- selection of vaccine strains
- engineering of RG vaccine strain



## OFFLU project in Indonesia

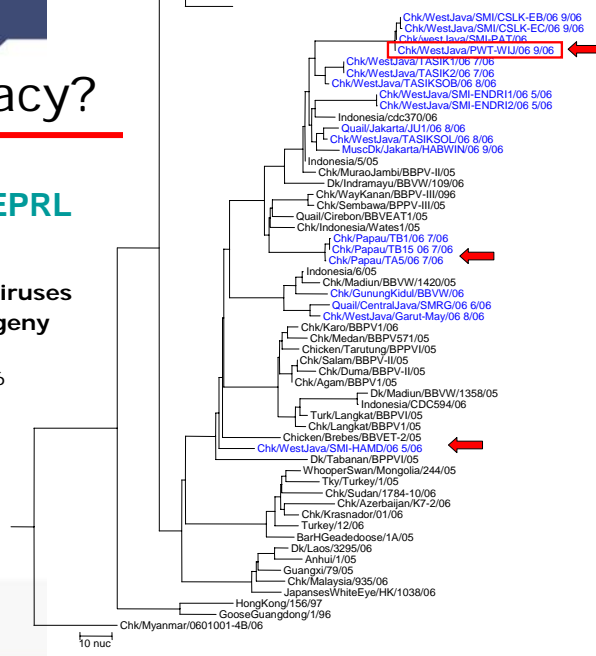




# Vaccine Efficacy?

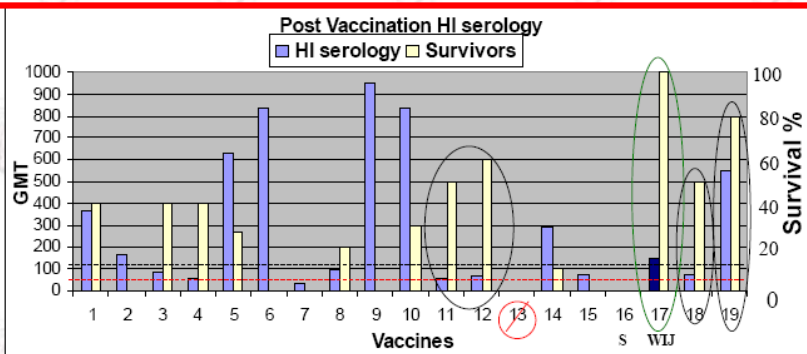
## AAHL and USDA/SEPRL

- Selection of 3 challenge viruses
- Selection based on phylogeny
  - A/ck/WJ/PWT-WIJ/06 9/06
  - A/ck/WJ/SMI-HAMD/06 5/06
  - A/ck/Papua/TAS/06 7/06

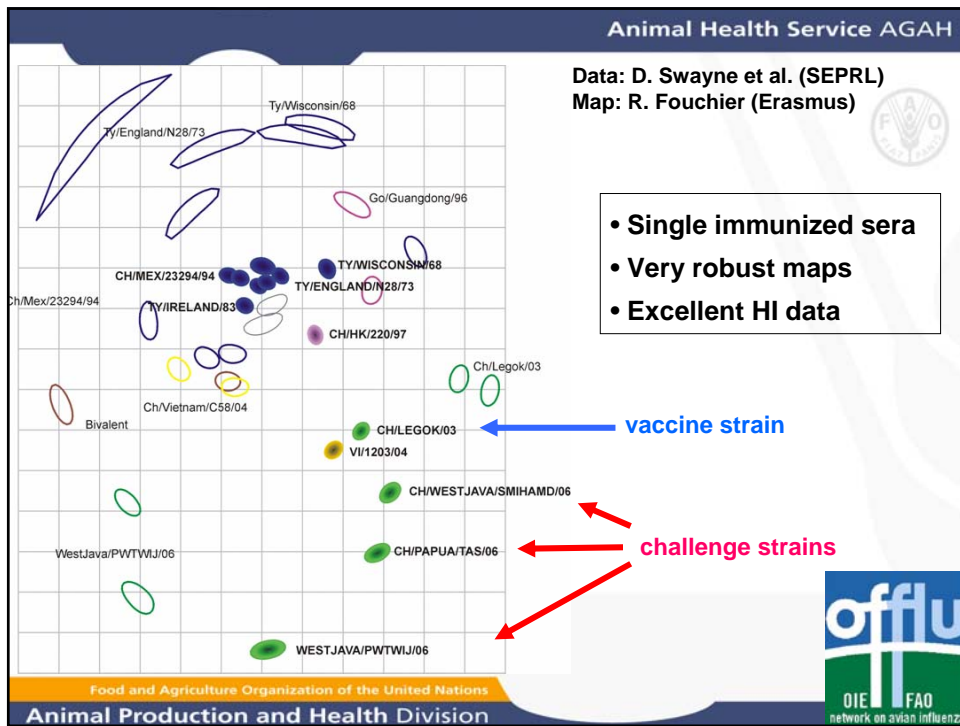


## Collaborative Vaccine Efficacy Project:

Vaccinated 1d (rFP-H5-AIV) and 3wks (Legok/03), or 3 wks (17 OE Vaccine); IN challenged 6 wks, 106 EID<sub>50</sub> IN of A/WJ/PWT-WIJ/06 (H5N1) HPAI virus, HI serology vax strain



- Excellent protection = WJ (Challenge control)
- Good protection = 19
- Marginal protection = 11, 12, and 18 (all H5N1 Eurasian lineage)
- No association between HI serology (Vax strain) and survival



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## OFFLU project in Indonesia

- 250 new viruses characterized (sequences to be deposited in public domain)
- Evaluation of antigenic cartography
- H5N1/H5N9 RG strain engineered and tested under the project. To be donated to Indonesian MoA
- Review of national vaccination strategy by the OFFLU group
- First experience. Should be applied to other countries

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network on avian influenza

## Main on-going OFFLU achievements



- Active collection of strains. Bridge between EU/FAO/other funded projects, the field and the scientific community including medical virologists
- 7 OFFLU technical groups:
- Contribution to establishment of a Unified Nomenclature System for H5N1 influenza viruses based on HA gene phylogeny (WHO/FAO/OIE, 2007)
- Evaluation of a new publicly accessible platform (EpiFluDB) in link with WHO
- OFFLU projects on vaccination in Indonesia and Egypt (implemented by FAO)
- Key role in this joint technical consultation on avian influenza at the human-animal interface

## Example of good animal-human interface



### • Kingdom of Saudi Arabia

Detection of specific mutations for humans in avian viruses (IZSve)

- e-mail from ISZVe to FAO CVO/OIE DG
- information forwarded to WHO ADG
- publication (in press)

*Journal of General Virology* (2008), 89, 000-000

DOI: 10.1099/vir.0.2008/004259-0

Short  
Communication

Co-circulation of two sublineages of HPAI H5N1 virus in the Kingdom of Saudi Arabia with unique molecular signatures suggesting separate introductions into the commercial poultry and falconry sectors

Isabella Monne,<sup>1</sup> Alice Fusaro,<sup>1</sup> Mohamed Hamad Al-Blawi,<sup>2</sup> Mahmoud Moussa Ismail,<sup>3</sup> Owais Ahmed Khan,<sup>4</sup> Gwenaëlle Dauphin,<sup>5</sup> Astrid Tripodi,<sup>5</sup> Annalisa Salvato,<sup>1</sup> Stefano Marangon,<sup>1</sup> Ilaria Capua<sup>1</sup> and Giovanni Cattai<sup>1</sup>

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Ilaria Capua  
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<sup>1</sup>Istituto Zooprofilattico Sperimentale delle Venezie, OIE/FAO and National Reference Laboratory for Newcastle Disease and Avian Influenza, Viale dell'Università 10, Legnaro, Padova, Italy  
<sup>2</sup>Veterinary Labs Administration, Ministry of Agriculture, Riyadh, Kingdom of Saudi Arabia



## Typical amino-acid signatures of human influenza viruses observed in KSA strains



Table 2. Typical amino acid signature of human influenza viruses observed in the Arabian strains

Protein	Position (aa)	Predicted aa		Viruses with detected mutations	Mutation	References
		Avian	Human			
PB2 NS1	627	E	K	All strains analysed in the present study A/otrich/Saudi Arabia/6732-3/2007 A/chicken/Saudi Arabia/6732-4/2007 A/turkey/Saudi Arabia/6732-6/2007 A/duck/Saudi Arabia/6732-7/2007 A/chicken/Saudi Arabia/6732-13/2007 A/chicken/Saudi Arabia/6732-18/2007	E627K E227K	Subhano et al. (1993), Chen et al. (2006) Chen et al. (2006), Finkelstein et al. (2007)
	227	E	R or K (H1N1 1918)			
PB1	327	R	K	A/otrich/Saudi Arabia/6732-3/2007 A/chicken/Saudi Arabia/6732-4/2007 A/turkey/Saudi Arabia/6732-6/2007 A/duck/Saudi Arabia/6732-7/2007 A/chicken/Saudi Arabia/6732-13/2007 A/chicken/Saudi Arabia/6732-18/2007	R327K	Chen et al. (2006)
NP	33	V	I	A/boubara bustard/Saudi Arabia/6732-1/2007 A/ikoon/Saudi Arabia/6732-2/2007 A/otrich/Saudi Arabia/6732-3/2007 A/chicken/Saudi Arabia/6732-4/2007	V33I	Chen et al. (2006)

## H5N1 in Africa (11 African countries)



### Genome Analysis Linking Recent European and African Influenza (H5N1) Viruses

Steven L. Salzberg,\* Carl Kingsford,\* Giovanni Cattoli,† David J. Spiro,‡ Daniel A. Janies,§ Mona Mehrez Aly,¶ Ian H. Brown,# Emmanuel Couacy-Hymann,\*\* Gian Mario De Mia,†† Do Huu Dung,‡‡ Annalisa Guercio,§§ Tony Joannis,¶¶ Ali Safar Maken Ali,## Azizullah Osmani,\*\*\* Iolanda Padalino,††† Magdi D. Saad,†††† Vladimir Savic,§§§ Naomi A. Sengamalai,‡ Samuel Yings†,†† Jennifer Zaborsky,‡ Olga Zorman-Rojs,¶¶¶ Elodie Ghedin,### and Iliaria Capua\*

- Strong correlation btw genetic clustering and area of origin
- Unique molecular signatures
- Reassortments in Nigeria
- Aa substitutions specific to human infections/drug resistance

### Evidence of Infection by H5N2 Highly Pathogenic Avian Influenza Viruses in Healthy Wild Waterfowl

Nicolas Gaidet<sup>1,2</sup>, Giovanni Cattoli<sup>3,4</sup>, Salha Hammoumi<sup>1</sup>, Scott H. Newman<sup>5</sup>, Ward Hagemeijer<sup>1</sup>, John Y. Takekawa<sup>1</sup>, Julien Cappelletti<sup>1</sup>, Tim Dodman<sup>1</sup>, Tony Joannis<sup>1</sup>, Patricia Gil<sup>1</sup>, Isabella Monne<sup>1</sup>, Alice Fusaro<sup>1</sup>, Iliaria Capua<sup>1</sup>, Shilovous Manu<sup>7</sup>, Pierfrancesco Micheloni<sup>8</sup>, Ulf Ottosson<sup>9</sup>, John H. Mshelbwala<sup>10</sup>, Juan Lubroth<sup>11</sup>, Joseph Domenech<sup>12</sup>, François Monicat<sup>13</sup>

<sup>1</sup>Centre de Coopération Internationale en Recherche Agronomique pour le Développement, Montpellier, France; <sup>2</sup>Instituto Zooprofilattico Sperimentale delle Venezie, Legnano, Italy; <sup>3</sup>Food and Agriculture Organization of the United Nations, Animal Production and Health Division, Rome, Italy; <sup>4</sup>Wetlands International, Wageningen, The Netherlands; <sup>5</sup>US Geological Survey, Western Ecological Research Center, Yuba, California, United States of America; <sup>6</sup>National Veterinary Research Institute, Vom, Nigeria; <sup>7</sup>FAO Level 10 Veterinary Research Institute, Jos, Nigeria; <sup>8</sup>Instituto Nazionale per la Fauna Selvatica, Bologna, Italy; <sup>9</sup>Ornisby Bird Observatory, Kellen, Luxembourg; <sup>10</sup>Federal Department of Forestry, Abuja, Nigeria

### Reassortant Avian Influenza Virus (H5N1) in Poultry, Nigeria, 2007

Isabella Monne,<sup>1</sup> Tony M. Joannis,<sup>1</sup> Alice Fusaro,<sup>1</sup> Paola De Benedictis,<sup>1</sup> Lami H. Lombin,<sup>1</sup> Hussein Ultram,<sup>1</sup> Anthony Egbuji,<sup>1</sup> Poman Solomon,<sup>1</sup> Tim U. Obi,<sup>1</sup> Giovanni Cattoli,<sup>2</sup> and Iliaria Capua<sup>1</sup>

Genetic characterization of a selection of influenza virus (H5N1) samples, circulating in 8 Nigerian states over a 10-month period in early 2007, indicates that a reassortment

isolation. We then characterized the entire genome.

Samples were processed using standard procedures (4-6). The gene segments was carried out (RT-PCR by using gene-specific primers). PCR products were sequenced using the ABI BigDye 3.1 sequencing kit (Applied Biosystems, Foster City, CA, USA). Phylogenetic analysis was performed using the neighbour-joining method as implemented in the Geneious software (6). GenBank accession numbers for the 12 Nigerian H5N1 sequences are EU714845-1.

As expected, all Nigerian H5N1 sequences were closely related to the viruses that have been reported from Europe, Russia, Africa, and Asia (7). According to the unique highly pathogenic influenza

## OFFLU at the animal-human interface



- Efforts made to communicate with the human side (information sharing, tripartite projects, emergency missions)
- Informal communication already in place but need to formalize it
- OFFLU group to improve mechanisms of key information sharing on viruses with human side (WHO-OFFLU staff)
- Efforts will be directed towards the recommendations of this meeting

## Acknowledgements

David Swayne and coll. (SEPRL)  
Peter Daniels and coll. (AAHL)  
Ilaria Capua and coll. (IZSve)  
Ian Brown and coll. (VLA)  
Ron Fouchier (Erasmus univ.)  
Elly Sawitri Siregar (CMU, Indonesia)  
FAO teams





Thank you for your attention!



## Strengthening OFFLU governance

- Executive Committee created
- Scientific Committee dissolved
- Open list of scientific contributors created
- Secretariat transferred to OIE
- OFFLU dedicated staff
  - 2 focal points: FAO (Sept 2006) and OIE (July 2007)
  - 2 OFFLU scientists: VLA (OIE, Nov 2007) and FAO (April 2008)
  - 1 secretariat