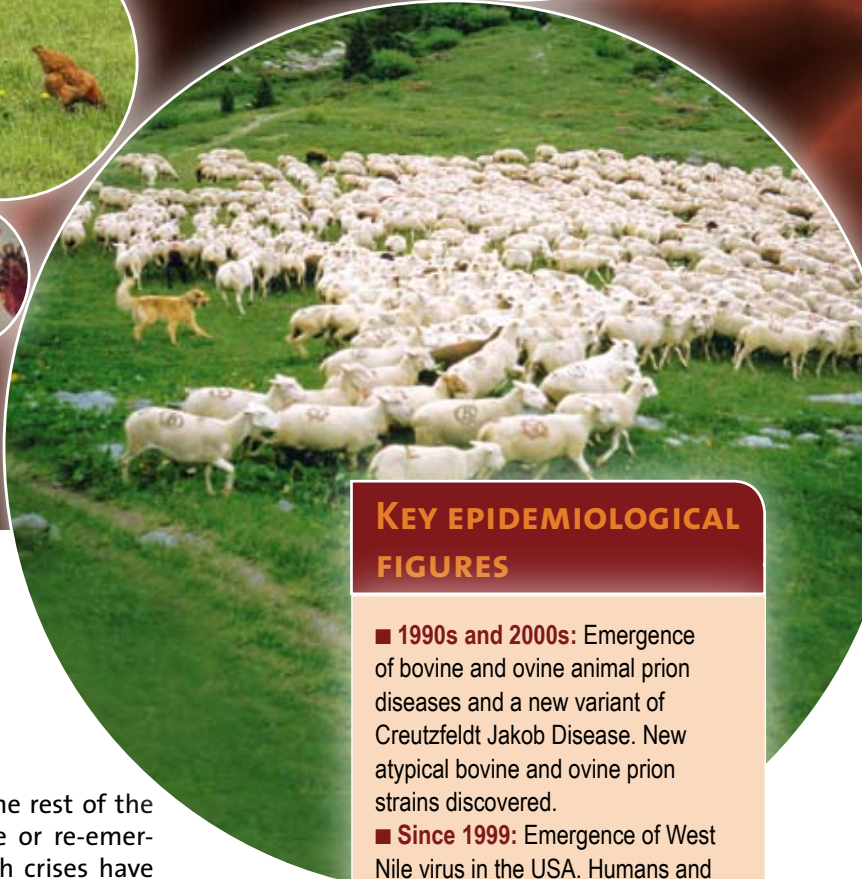


Emerging infectious animal diseases



French
Agricultural
Research
Center
for
International
Development



Renewed need for targeted research

In the past decade, rapid changes in France and the rest of the world have been accompanied by the emergence or re-emergence of infectious animal diseases. Recent health crises have brought to light the very real threat these zoonoses pose to human health, global food safety and the economy, stressing the need for revitalising research in this area. Infectious disease control and preparation for epidemics depend on research and innovation that are based on scientific knowledge and findings from various fields of expertise.

While each situation is highly specific, the underlying scientific questions remain the same: adaptation of infectious agents and vectors, animal immune response, genetic variability, host and vector biology and ecology, and modelling the occurrence and spread of diseases, etc. In addition, recent outbreaks of avian flu and bluetongue disease have demonstrated North-South interdependence in terms of animal and Public Veterinary Health.

The combined efforts of CIRAD and INRA, along with their partners in research, training and development, have provided the means to address the animal health issues facing the world and to strengthen the position of French research in the international community.

Marion Guillou
President of INRA

G rard Matheron
Director General of CIRAD

KEY EPIDEMIOLOGICAL FIGURES

- **1990s and 2000s:** Emergence of bovine and ovine animal prion diseases and a new variant of Creutzfeldt Jakob Disease. New atypical bovine and ovine prion strains discovered.
- **Since 1999:** Emergence of West Nile virus in the USA. Humans and horses are accidental hosts.
- **2001:** Foot and mouth disease outbreaks in the United Kingdom and France.
- **2002:** SARS epidemic probably linked to virus transmission between bats and the civet cat, a small carnivorous mammal.
- **Since 2004:** Human cases of avian flu due to close contact with domestic birds. Continuing risk of a pandemic.
- **Since 2006:** Emergence of two ovine bluetongue viruses in ruminants in mainland France.
- **2007:** Rift Valley Fever epidemics in East Africa, Madagascar and Sudan, affecting both human and livestock populations.
- **Since 2008:** Emergence of *Peste des Petits Ruminants* in the Maghreb, threatening Europe.

The positions of risk managers

Emerging and re-emerging animal diseases: The role of the French Directorate General for Food

Environmental and health issues are a frequent cause of concern to both the general public and the health authorities, particularly when confronted by animal diseases previously unknown or re-emerging in the country, and especially those that can be transmitted to humans. Veterinary services are responsible for ensuring the health of livestock in France, for both economic and health reasons. Indirectly, this involvement also affects the preservation of the countryside.

The Directorate General for Food (DGAL¹), conscious of the need for a coordinated, multidisciplinary approach, actively seeks to involve the different stakeholders in monitoring, surveillance, warning systems and disease-prevention programmes, and ensures that national policies remain in step with those of the EU and the international community. It also supports research and studies carried out in this field.

In France, the DGAL has recently supported the creation of the French network for animal health where farmers and veterinarians can discuss their needs and expectations with researchers from institutes such as INRA and CIRAD, and with the research and development teams of pharmaceutical firms.

During the French EU presidency, the DGAL also supported plans to create a Euro-Mediterranean animal health network to pool projects from the EU and the countries of the Mediterranean basin. Rapid detection and transparent notification of outbreaks to international organisations such as the OIE² are essential conditions for controlling the spread of disease. ■

Monique Eloit

Deputy Director General for Food
Head of veterinary services
FRANCE

Protecting the planet from emerging diseases related to globalisation

Improving the management of public and private animal health systems world-wide is the best way to tackle the unprecedented impact of emerging and re-emerging animal diseases and zoonoses. Recent epizootic crises have shown how coordinated policies and appropriate animal health programmes can improve public health, including food safety. What is required above all is the early detection of foci and the rapid response of national veterinary services. During the avian influenza crisis, the OIE recommended strengthening veterinary governance world-wide as part of a Global Public Good approach. The entire planet could be imperilled by a single country without the necessary resources.

With the support of the World Bank, the European Commission and all its member states, the OIE has listed as one of its top priorities good governance in animal health, most notably by helping developing or transition member countries to upgrade their veterinary services to the organisation's quality standards. The programme to evaluate the performance of veterinary services has helped strengthen the means to tackle health risks world-wide.

To achieve this, research policies, as well as major research bodies like INRA and CIRAD and their partners, must ensure that innovations and data on mechanisms of emergence are made available so that appropriate tools, suited to diverse ecosystems, can be implemented to preserve animal health and prevent and control animal diseases. ■

Bernard Vallat

Director General of the World Organisation
for Animal Health (OIE)

¹ *Direction générale de l'alimentation – French Ministry of Agriculture and Fisheries*

² *World Organisation for Animal Health*

«Emerging diseases highlight the need for appropriate research organisation»

For a stronger impact on the international scene, INRA and CIRAD have joined forces to increase and pool their resources in specific, integrated disciplinary areas: parasitology, virology, animal immunology, veterinary entomology, pathology, epidemiology and modelling, health ecology and, most recently, health economics. This strategy takes the form of partnerships with national veterinary schools, universities and AFSSA, as well as the creation of large-scale research collectives.

In recent years, major areas of research on prions, avian influenza, tick-borne diseases and Bluetongue disease have been developed and become the focus of collective action. The high international profile and the competitiveness of research teams working on emerging diseases require access to high throughput technologies, bioconfinement facilities and monitoring and observation networks. INRA and CIRAD have thus set up several shared European and international tools, such as the Institute of Animal Infectiology Experimentation/Institut d'expérimentation en infectiologie animale (Animal infectious disease research institute), including INPREST (Installation Protégée pour l'Etude des Encéphalopathies Spongiformes Transmissibles/TSE research facility), and CaribVet, an animal health monitoring and research network in the Caribbean.

These projects all form part of a European and international perspective, and are a component of a more global approach to health economics and ecology and the integrated control of infectious diseases.

Collective tools to address health issues at European and world levels

■ CaribVet, the Caribbean Animal Health Network: combining research and monitoring

The Caribbean is a fragile tropical area which is a hub of international trade, with a high risk of the emergence of infectious diseases and pathogens. Over the last ten years or so, CIRAD has been developing a regional animal health network there. Known as CaribVet, its goal is to help harmonise and strengthen the monitoring and control of animal diseases at the regional level, based on infectious diseases and epidemiological

research findings. In 2006, CaribVet was officially recognised by Caricom and the OIE as the official Caribbean animal health network. The CIRAD-INRA CMAEE joint research unit provides the methodological foundations and coordinates the activities of specific working groups (epidemiology, diagnostics and quality control, avian influenza, classical swine fever, ticks and tick-borne diseases, rabies, salmonellosis and leptospirosis) that

draw up standardised protocols for the region. The www.caribvet.net website is a major information tool used by the network. The CMAEE unit is also responsible for the OIE reference laboratory for cowdriosis, a tick-borne disease. The network draws its success from the fruitful interaction of monitoring and research, backed by dynamic, internationally recognised research.

■ The Institute of Animal Infectiology Experimentation/The Institut d'Expérimentation en Infectiologie Animale (Institute for animal infectious disease research) (IEIA) and the INPREST facility for TSE research

Experimentation is one of the foundations of infectious disease research. However, it has to meet new challenges: cost-effective and ethical demands, stricter regulatory and health restrictions, and new experimental paradigms. In 2002, with the emergence of prion diseases, the Ministry of Agriculture asked INRA to participate in overhauling the infectious disease research facilities in France. INRA, the state, and other French partners invested in

modern facilities for INRA (€18M up to 2012) suited to the methodological demands of infectious disease experimentation on terrestrial (from mouse to cattle) and aquatic animals, with high bioconfinement levels (A3, A3+ for high-security isolation facilities). In 2008, the Animal Infectious Diseases Experimental Institute was created. It includes INPREST, Bio Secure containment facilities for transmissible spongiform encephalopathy research. The ISO-9001 and

IBISA (Infrastructure in Biology, Health and Agronomy) facility is open to the French and European scientific community from both the public and private sectors. It provides CIRAD and its partners with the means to carry out experiments on infectious diseases from the South. In 2008, INRA launched a project (NADIR) to coordinate fourteen similar major European facilities, funded by the European community (€8M).



Examples of INRA-CIRAD research on emerging animal diseases

■ Avian influenza

Since 2005, INRA and CIRAD have been developing research on avian influenza (highly pathogenic avian influenza in birds, avian influenza in humans). An «influenza bureau» was established by INRA's Animal Health Division (DSA) to coordinate the research of the institute and its partners.

The bureau brings together INRA, CNRS, CIRAD, AFSSA and the Pasteur Institute. Research, supported by INRA and CIRAD teams, covers viral biology and diversity, cell and immunopathological response of hosts (murine, poultry and palmiped models), vaccine innovation and strategies, epidemiology and interaction with wild fauna.

Coordination between the DGAL, INRA and AFSSA has been formally established since 2008 through an agreement including the creation of a special €2M fund. INRA is responsible for managing the fund and for the secretariats of the steering committees and scientific advisory board. In 2008, three research areas were covered: low-pathogenic strains, viruses and environments, and means of prevention and control. Coordination between INRA and the Pasteur Institute takes the form of joint programmes and is found in an Ile-de-France regional programme: «Emerging infectious diseases» (€4.5M).

INRA and CIRAD teams are involved in 60% of French National Research Agency projects on avian influenza. Finally, CIRAD is part of international monitoring efforts in conjunction with the OIE and the FAO.

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RU 892 VIM, Jouy-en-Josas

■ Bluetongue: spreading north to Europe



Bluetongue disease, or Bluetongue fever, is a viral disease affecting domestic and wild ruminants. The twenty-four known Bluetongue viruses (BTV1 to 24) are transmitted by insects (*Culicoides spp.*).

The disease used to be found only in hot climates, but by 2000 it had made its way up to Corsica several times, with different virus types.

These infestations were linked to the northward spread of *Culicoides imicola*, the main carrier of these viruses in Africa. Both carrier and virus were placed under close surveillance in the Mediterranean basin. In 2006, Bluetongue appeared in northern Europe with a type 8 virus, not observed in the Mediterranean basin. This triggered a major health crisis that increased in France and Europe in 2007 and 2008.

A type 1 virus arrived via south-west France in 2007, and a type 6 virus appeared again in northern Europe in 2008. None of these introductions, however, were related to the arrival of the expected vector *C. imicola*. It is still unknown how these viruses entered the country, but they may have been transmitted by local *Culicoides* species, allowing the disease to become established.

These observations highlight the need for research on the plasticity of microorganisms and carriers and how they adapt to environmental changes.

It stresses the importance of developing innovative vaccine-based control methods, based on detailed knowledge of immunological and pathological mechanisms - research conducted by INRA and CIRAD with their partners.

Dominique Martinez
CIRAD, Director of the CIRAD-INRA
CMAEE JRU, Montpellier

■ Ticks and tick-borne diseases

Ticks are ectoparasites of domestic and wild animals. They transmit pathogens causing diseases with a strong economic impact. These arachnids are very common in inter-tropical areas.

Due to environmental changes, tick populations have been growing in temperate regions, where they transmit viruses (tick-borne encephalitis), bacteria (*Bartonella*, *Anaplasma*) and parasites (*Babesia*) to wild and domestic animals and even humans.

Consequently, the study of tick biology, the pathogens they transmit, and the diseases caused are among the joint priorities of INRA and CIRAD.

Since 2007, the Animal Health Division has launched a series of projects aimed at studying the interactions between pathogens, vectors and mammalian hosts, population genetics (carriers and transmitted pathogens) and the epidemiology of transmitted diseases.

The project on the «dynamics and genetic diversity of tick populations and transmitted pathogens: a comparative approach of tick-pathogen pairs in temperate (*Ixodes/Bartonella*) and tropical (*Amblyomma/Ehrlichia*) areas» studies two models of particular relevance to human and animal health.

It reinforces other actions, both national (Génoscope project, *Ehrlichia* genomics) and international (European project - epidemiology and development of new-generation vaccines for *Ehrlichia* and *Anaplasma* - CRVOI project, genetics and dynamics of *Amblyomma* tick populations and *Ehrlichia*), coordinated by the CIRAD-INRA CMAEE JRU.

Olivier Plantard
INRA, INRA ENVN BioEparJRU, Nantes



■ **Enzootic infectious and parasitic diseases**

Emerging diseases and epizootics should not obscure the fact that enzootic infectious diseases remain the greatest health concern in livestock in both the North and the South. In the North, mastitis is the most widespread disease in dairy cows. Q fever, which leads to abortions in sheep, can be transmitted to humans via aerosols. Paratuberculosis is a chronic infection that can have a devastating effect on ruminant livestock farms. Tuberculosis is still endemic in some European countries. *Salmonella* and *Campylobacter* are the main causes

of human food poisoning (350,000 cases in Europe in 2007 – EFSA, 2009). In the South, tuberculosis, brucellosis, anthrax, swine fever, *Peste des Petits Ruminants*, and foot and mouth disease continue to be significant health and economic concerns for livestock farmers, and in some cases constitute public health hazards. In temperate or inter-tropical areas, there are recurrent multifactorial health problems – respiratory diseases, digestive disorders, neonatal diseases and parasitic infections. How to deal with these enzootics remains one of

the main concerns of the production sector. Control methods are complex and require basic or applied research, combining research and extension services. INRA and CIRAD are strongly committed to these goals.



Examples of animal infectious disease projects jointly supported by INRA and CIRAD

Since 2008, INRA and CIRAD have set up a series of cross-disciplinary projects to optimise collaboration on infectious animal diseases between various research entities, in addition to existing partnerships in projects financed by the French National Research Agency or the EU framework programme for research and technological development.

Dynamics and genetic diversity of tick populations and transmitted pathogens: a comparative approach of tick-pathogen pairs in temperate (*Ixodes/Bartonella*) and tropical (*Amblyomma/Ehrlichia*) areas

UMR 1309 CIRAD INRA CMAEE, CIRAD UPR 22 AGIR, UMR ENVN / INRA BioEpar ; UMR 956 ENVA / Afssa / INRA / Univ BIPAR, INRA UR 346 EpiA

Generic tools for the study of the pathogenicity of ruminant mycoplasmas

UMR 1090, INRA, Univ. Bordeaux 2, UMR1225, INRA/ENVT, C. Citti, Toulouse; UMR 1309 CIRAD INRA CMAEE

Modelling of vector-borne diseases: inclusion of spatial components in a model of the dynamics of a metapopulation of vectors

CIRAD UPR 22 AGIR, UMR ENVN / INRA BioEpar

Molecular characterisation of ruminant paramyxovirus nucleoprotein and its application in the development of improved vaccines

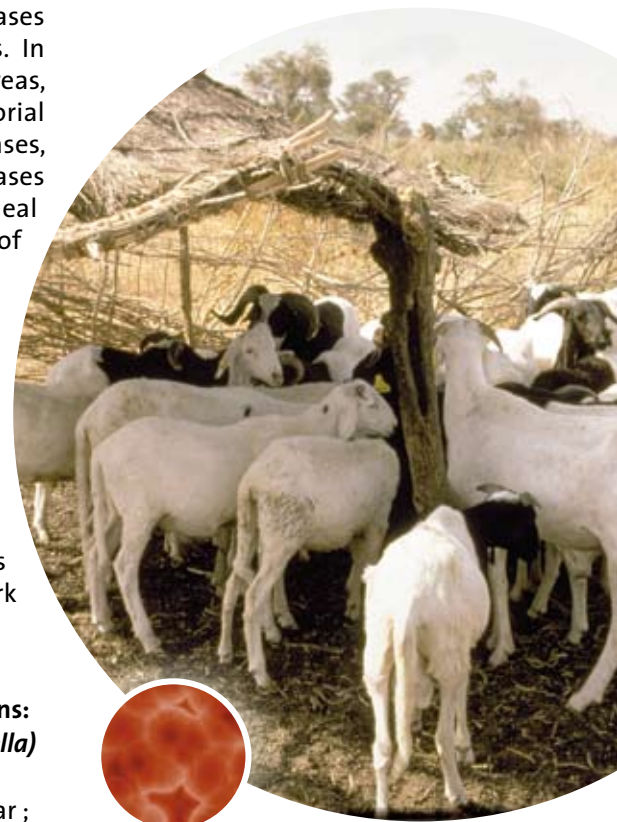
INRA UR 892 VIM, UMR 1309 CIRAD INRA CMAEE

Use of biotinylated viral vectors to target ruminant dendritic cells in order to modify their cytokinetic orientation and/or cause expression of antigens with vaccine potential

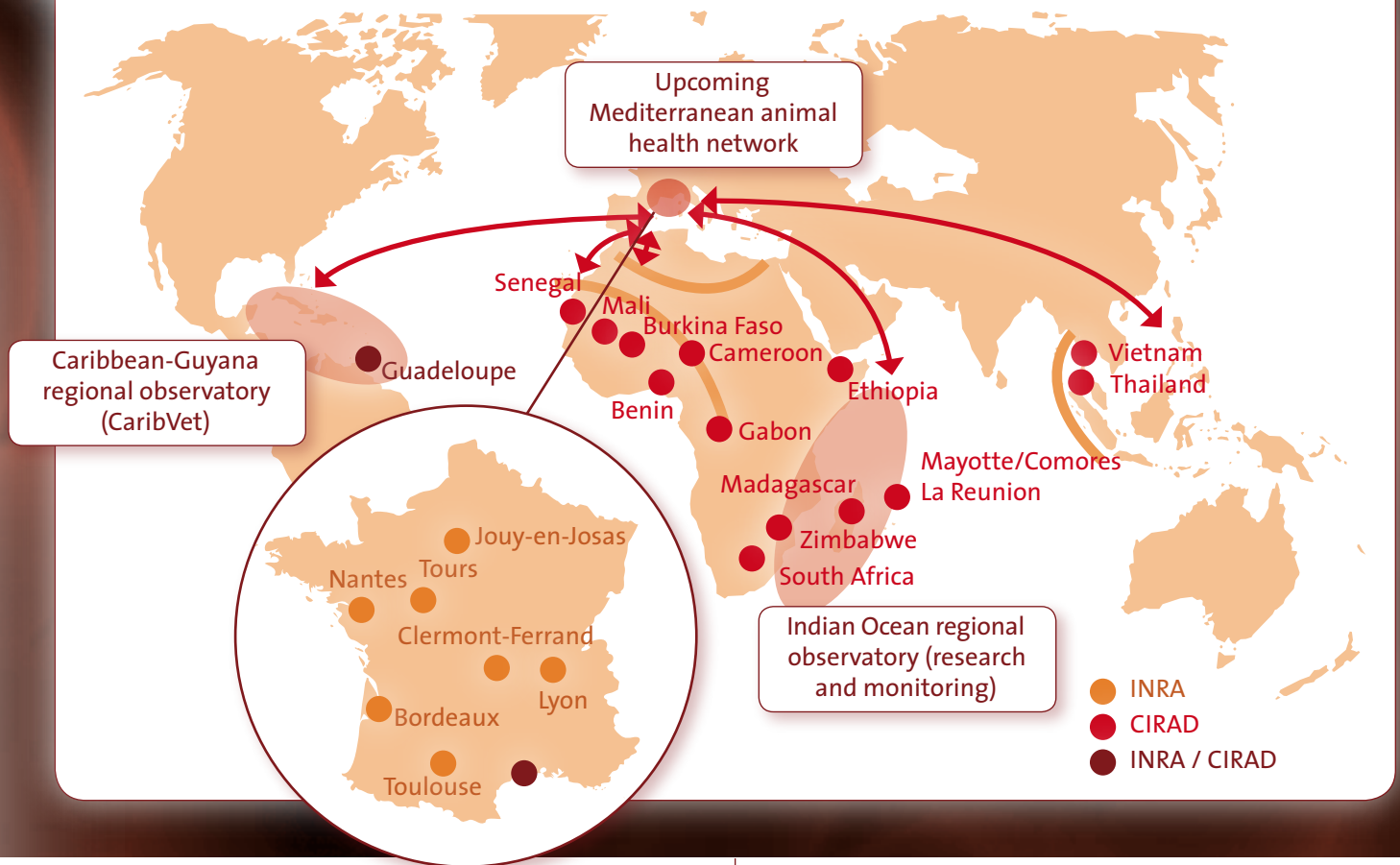
UMR 1161 INRA – Afssa – ENVA Virologie, INRA UR1282 IASP, CIRAD UPR15

Health geography: Study of the role of social and economic factors in the persistence of H5N1 avian influenza in Thailand

CIRAD UPR 22 AGIR, UMR ENVN / INRA UR 346 EpiA



INRA and CIRAD sites for animal health



■ INRA and CIRAD Partnerships

European coordination
 Rex (network of excellence): Eadgene (host-pathogen interactions)
 PI (integrated project): Eden (emerging diseases and environmental changes)
 Nadir (animal infectious disease facilities)
 Era Net Emida (emerging and major infectious diseases of livestock)
 SCAR – WG Animal health and Welfare
 MedReoNet: surveillance of Reoviruses (Bluetongue and African Horse Sickness)
 Participation in networks of excellence: EpiZone, MedVetNet, NeuroPrion

■ Professional partners in the areas of animal health and veterinary public health

Académie vétérinaire de France
 Directorate-General for Food (Ministry of Agriculture and Fisheries)
 Directorate-General for education and research (Ministry of Agriculture and Fisheries)
 École nationale des services vétérinaires
 France vétérinaire international
 IE, IFIP, ITAVI, Haras nationaux
 World Organisation for Animal Health (OIE)
 Food and Agriculture Organization (FAO)
 French network for animal health
 Syndicat de l'industrie du médicament vétérinaire et du réactif (SIMV) and its members
 FNGDS and GTV (and their regional organisations)
 UNCEIA, EID

■ Partnerships through European networks

European Technology Platform for Global Animal Health
 Wageningen University Research, Royal Veterinary College, Liège University, Utrecht University, BCSRC
 Surveillance networks for the South:
 CaribVet, Indian Ocean, CRVOI (Centre de recherche et de veille de l'Océan Indien)
 Reference laboratory for OIE, FAO, DGAL

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