

# Animal lab protects people





**The Netherlands is affected by more and more infectious animal diseases such as avian flu which can make people ill too. In order to do thorough research on this, a lab is being built at which live infected farm animals will be kept. No virus can escape from the lab. 'Even the DNA is destroyed.'**

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**A**t the end of last year when a highly pathogenic strain of avian flu broke out on four poultry farms in the Netherlands, it was 'all hands on deck' at the Central Veterinary Institute, part of Wageningen UR. The laboratory in Lelystad was working overtime to check all the specimens from poultry farms for the highly infection H5N8 virus. There were strict safety protocols for the analysis of the specimens in the lab to prevent the virus from escaping or infecting the analysts.

The avian flu is a zoonosis: an infectious disease that can be transferred from animals to humans and thus have human victims. Other familiar examples are BSE, mad cow disease and Q fever. An outbreak of Q fever has struck thousands of people since 2007, most of them living near goat and sheep farms. Research by the CVI delivered insight into this disease and its epidemiology which helped in fighting it.

'We also want to be prepared for the arrival of new zoonoses in Europe,' says director Andre Bianchi. He cites the Rift Valley virus, the West Nile virus and the Crimean-Congo virus (see box). 'We are experiencing a lot more threats now,' says Bianchi. 'Two thirds of infectious diseases can infect both animals and people.'

For this reason, on top of its existing laboratories for exposing the presence of diseases, the CVI is building an extra secure shed for housing test animals with infectious diseases. Here, researchers can infect chickens, pigs, sheep and cattle with a zoonosis and monitor the behaviour of the dangerous disease in the animal, how it spreads within a group and whether vaccination is possible. This is the first laboratory in the Netherlands in which zoonosis research can be done on large farm animals. The ministry of Economic Affairs, Agriculture and Innovation has contributed to the costs of the building (as did the province of Flevoland), and of the research.

#### **DNA DESTROYED**

The new national facility was opened in February. At first glance, the lab is not much more than an experimental shed. Once inside, it becomes clearer why the building cost 9.5 million euros. Because not a single pathogenic bacterium or virus must be allowed to escape the research facility, all the manure, bedding and water is destroyed in special destructors in the cellar of the lab. The corpses of the animals themselves are also treated in

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## NEW THREATS

Besides known zoonoses such as the highly pathogenic avian flu and Q fever, there are new infectious diseases threatening the Netherlands. The top 3 according to the CVI:

**Rift Valley Fever** is caused by infection with a virus found in cows and sheep, and is spread by insects and the blood and milk of infected animals. People infected with the disease can suffer headaches, bleeding and liver problems. The disease originated from the Rift Valley in Kenya, but in recent years has been heading for Europe via North Africa.

**The West Nile virus** is another insect-borne disease which originated in Uganda but is already present in Algeria, Romania and the United States. In the United States the disease killed nearly 300 victims in 2012. The virus is found in mammals, birds and humans and is already endemic in countries around the Mediterranean.

**Crimean-Congo fever** comes about through infection with a virus transferred from animals to humans by ticks. In humans it can lead to bleeding, high fever and in some cases, death. The virus can develop in cattle, sheep and goats, which do not fall ill themselves. The *Hyalomma marginatum* tick, common in Africa, Asia and eastern Europe, is the main carrier of the disease. The tick has now advanced to just south of Paris.



a large destructor with a combination of high temperatures, high pressure and acids until nothing remains of a sheep or pig but a dough-like lump. 'Even the DNA is destroyed,' says Henk Sloetjes, head of the department of Animal Health and Biotechnology at the CVI. The price of this machine alone: 1 million dollars.

The building is also equipped with extensive facilities for preventing viruses or bacteria from escaping from the lab or infecting the staff. Everyone entering must undress completely, for instance, and don clothing and underwear provided by the CVI. Before entering infected rooms, researchers put on boots, protective clothing and masks. To enter the building they have to go through three chambers, each sealed off with submarine doors, before they reach the stalls. The doors can only be opened with a code and a finger vein ID – the unique pattern of veins in a fingertip. The doors only open in turns so that the air cannot move between the chambers, while negative pressure ensures that no air passes from the infected area to the clean area. Moreover, all the air in the chambers is purified before the staff come from the barn to the clean area.

After visiting an infected space – a stall, the operation or dissection room – the researchers take their boots off, rinse their protective clothing with disinfectant, hang them up and throw out the clothes they had on under it. In the next room it is compulsory to shower for three minutes, after which they can get dried and dressed.

### HIGHEST SAFETY LEVEL

Security in research laboratories working with infectious diseases is expressed in the Bio Safety Level (BSL). There are four safety levels, with BSL4 imposing the highest safety standards, which ensure that viruses and bacteria cannot spread. A distinction is made between the safety of the staff, indicated with the letter h, and that of the animals, indicated with a v. The new facility for zoonosis research at the CVI has safety levels h-BSL3 and v-BSL4. The safety level at the CVI is there-

fore not high enough to treat ebola patients, explains Bianchi. Protection against that extremely infectious disease requires the highest human Bio Safety Level, h-BSL4. ‘You need that level of safety when there is a high risk of death from the infection. If that risk is lower, or if vaccines or antibiotics are available that can prevent or cure the disease, then safety level 3 is enough. That applies to our research on rabies, for example, a very nasty infectious disease in mammals. The colleagues doing that research have been vaccinated against the disease.’

Working with high-risk animal diseases is nothing new for the CVI. Since the nineteen seventies, the institute has been studying diseases such as foot and mouth disease in a High Containment Unit. ‘Foot and mouth disease is a highly infectious disease affecting cows, but is not dangerous for humans. So safety level h-BSL2 was enough. We could also do research on swine fever and the low pathogenic avian flu, which are not dangerous for humans either. But in the last 10 years we have been faced by more and more zoonoses such as Q fever and the high pathogenic avian flu. Research on these animal diseases has to be done in an h-BSL3 lab. For that we created a couple of labs with extra protective measures for the staff within our existing facilities. In these labs we could already do lab tests with diseases such as avian flu and Q fever, but not with live infected farm animals. We also had to go to great length to keep things safe when we did dissections on infected animals and when transported infected material off the site. All that is much better organized now that we have brought the stalls, the dissecting room and the destruction process under one safety regime.’

### TESTING VACCINE

Bianchi expects an increase in demand for research and knowledge on zoonoses. ‘It will be a matter of establishing what type of virus we are dealing with, where it lodges in the animal, how a virus or bacterium spreads and how to develop a vaccine.’

‘We are increasingly  
having to deal with  
zoonoses’

In the new facility the CVI can track down pathogens faster and better and can test vaccines on pairs of animals. In the first instance, vaccines need to ensure the animals no longer fall prey to the disease, explains Bianchi, but it also needs to be made clear whether the virus can spread via the vaccinated animal. ‘We can test that now by infecting vaccinated animals with the zoonosis and then introducing it into unvaccinated animals.’

The national facility is not intended exclusively for CVI researchers but also for veterinary researchers at Utrecht University, for example, and virologists at the Erasmus Medical Centre in Rotterdam. One of these is flu researcher Ron Fouchier, who heads the national influenza centre in Rotterdam. Fouchier already has very secure facilities for research on zoonoses such as avian flu.

‘In our facility we can do tests on chickens or ferrets in cages but not on large farm animals like pigs. So the new facility in Lelystad is a good addition for our joint research. Now we can do better research on swine fever, for instance.

Fouchier collaborates with the CVI on avian flu, with the CVI focusing on research and diagnosis of the virus in poultry and Fouchier on monitoring wild birds that could transmit the disease. He also supervises, together with the CVI, a PhD researcher who is investigating why one avian flu virus spreads so much more easily among poultry than another. ‘We have a strong overlap in expertise, but we are collaborating better and better so as to pool all the knowledge on zoonoses.’ ■

[www.wageningenur.nl/cvi/zoonoses](http://www.wageningenur.nl/cvi/zoonoses)

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## WAGENINGEN ACADEMY

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For an update on knowledge about controlling infectious animal diseases, Wageningen Academy offers a course on Epidemiological tools for controlling infectious animal diseases.

**For more information see [www.wageningenacademy.nl](http://www.wageningenacademy.nl)**

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