Mission report:

Training Workshop on the analysis of Turkish and Iranian (GIS-VET) FMD data: Ankara 14-18 March 2011

Ankara, Turkey (14 – 18 March 2011)

By Theo Knight-Jones, consultant veterinary epidemiologist to EuFMD
25th March 2011

Course run by Dr Melissa Mclaws, Dr Chris Bartels and Mr Theo Knight-Jones with inputs from Ettore De Maio and Dr Sergei Khomenko
Executive summary

Recommendations:

1. Continue to develop data sharing protocol between Iran and Turkey, as leaders for the W. Eurasia region
   a. Each country should provide a sample of data to Ettore by April 4 to allow him to develop a sample report. Further discussion can take place at the EuFMD general session
2. Provide follow-on training in statistics and epidemiology (including in Stata) for a small group of Turkish and Iranian veterinarians
   a. This may be done through online courses and/or further training courses by EuFMD/FAO
   b. Further courses involving both countries may be considered if desired by both Iran and Turkey
   c. Other training courses could also be offered, if desired (eg GIS)
3. In close consultation with the workshop participants, EuFMD epidemiologists will continue to analyse the data provided during the training courses with the aim to:
   a. Describe 2010 epidemic
   b. Explore the relationship between outbreaks and vaccination
EuFMD will procure Stata for use in the Phase 3 FMD project in Iran

The workshop consisted of five major areas which are discussed below.

Training in data analysis with Stata
The workshop lasted for four and a half days and roughly half the time was devoted to data analysis training. This was enough time to tackle some of the very basics of using Stata (the statistical software package used in the workshop) but little more. To further progress will require not only more technical training with Stata but also training on relevant epidemiological concepts.

However, it appeared that both countries could see the use and power of such software and were eager to learn.

Stata software licences will need to be purchased in the future.

For future training in this area, it is strongly recommended that the appropriate people attend and that these same people then attend subsequent training workshops.

Data analysis and data acquisition
By the second day the Iranian data was ready for analysis. The Turkish data was not ready until near day four (and some of the data needed a lot of cleaning). For this reason more progress was made on analysing the Iranian data than the Turkish (see appendix 6 for initial Iranian data analysis). Some insights were gained into possible spatial analysis that could be done and current factors limiting this spatial analysis.
Importantly the relevant data (including Turkey and Iran outbreak, vaccination and livestock population data) was made available and more analysis will be done imminently. Outcomes of this analysis will follow.

**Data sharing**

Both countries were keen to share data, although the people to authorise this data sharing from the Turkish side were not present. Useful discussions were made on the format and type of data that should be shared.

The meeting produced a recommendation on data fields to be submitted on a monthly basis to FAO, which will use the Empres-i system to produce an automated monthly report accessible to parties agreed by the project partners (initially Iran, Turkey and FAO). The countries should send a sample of the recommended data to Ettore as soon as possible to produce a sample report for the decision makers to discuss. A summary of the meeting recommendations regarding data sharing are provided in Appendix 7.

It is hoped that these two countries will lead the way for data sharing in the region.

**Serological studies in Iran**

Due in part to the understanding that Razi vaccines widely used in Iran are not purified and might induce an NSP antibody response, no extensive sero-surveys have been done in Iran in recent years. However, experience in other countries shows that sero-surveys can provide useful information even when impure vaccines are used, and indeed are necessary to gain a good understanding of the true distribution of FMD infection. A number of possible studies to be done to investigate this area were proposed in a previous mission report by Chris Bartels. These were reviewed with input from the Turkish experience by Naci Bulut and it was agreed to redraft the proposals in a clear fashion with table and diagrams.

**Turkish and Iranian outbreaks in 2010**

An excellent overview was provided on the FMD situation in the two countries. The Turkish presentation was particularly detailed, describing the problem of different strains to which the livestock population was immunologically naive. Details of sero-surveillance in Turkey were also provided.

A major point for discussion in Iran is the proposed theory that vaccination is actually predisposing epi-units to outbreaks by causing transient immune suppression. The data required to confidently analyse this was not available (available data has numerous limitations and biases that prevent immediate analysis of this problem). However, this theory is not supported by current scientific knowledge. More outbreaks might be observed around vaccinated premises because 1) high-risk premises are vaccinated preferentially and 2) vaccine delivery might spread disease if herds incubating FMD are vaccinated. Iran will no longer practice ring vaccination around outbreaks, but increase biosecurity and quarantine practices because of this putative problem.
4. Acknowledgements

We are very grateful to the Şap institute and in particular Dr Naci Bulut, for hosting this workshop and to the Iranian and Turkish veterinary authorities for participating and providing access to such useful FMD data. We are also indebted to staff at EuFMD for much of the logistic arrangements.
Objectives:

Objectives
1. Review and collate data available for analysis
2. Descriptive analysis of outbreaks, vaccination, serology data
3. Preliminary risk factor analysis:
4. At end of workshop, have a plan for next steps for additional analyses
5. Training: introduction to analytical epidemiology for participants
   a. Provide resources for further study/work
   b. Encourage participants to continue analyses after the workshop
6. Promote regional data sharing (Ettore De Maio)
7. Design study to assess role of wild boar in FMD transmission (Sergei)

Time table

Flexibility was key to workshop but the following outline was produced.

<table>
<thead>
<tr>
<th>Day 1 Monday</th>
<th>morning</th>
<th>afternoon</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Introductions:</td>
<td>• Small group work: loading data into stata and data cleaning</td>
</tr>
<tr>
<td></td>
<td>• Review objectives, agenda</td>
<td>Include discussion on bias/representativeness of data</td>
</tr>
<tr>
<td></td>
<td>• Presentation: software (Stata)</td>
<td>All</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2-4 can work with Ettore</td>
</tr>
<tr>
<td>Day 2 Tues</td>
<td>morning</td>
<td>• Presentation: descriptive analysis</td>
</tr>
<tr>
<td></td>
<td>• Define research questions that can be worked on given the dataset(s) available</td>
<td>TKJ</td>
</tr>
<tr>
<td></td>
<td>• Small group work: descriptive analyses (or one research question for one person)</td>
<td>All</td>
</tr>
<tr>
<td></td>
<td>afternoon</td>
<td>2-4 can work with Ettore</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Small group work: descriptive analysis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o Prevalence (outbreak reports, infection)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o Vaccine coverage</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o Mapping of prevalence and vaccination coverage</td>
</tr>
<tr>
<td></td>
<td></td>
<td>All</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td></td>
</tr>
<tr>
<td>Day 3 Wed</td>
<td>morning</td>
<td>Small group work: develop causal diagram</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Small groupwork: univariable associations</td>
</tr>
<tr>
<td></td>
<td>afternoon</td>
<td>All</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2-4 can work with Ettore</td>
</tr>
<tr>
<td>Day 4 Thurs</td>
<td>Morning</td>
<td>Preparation of presenting descriptive analyses results, interpretation and conclusions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Present findings to whole group/discussion and next steps</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Small groupwork: Multivariable analysis to determine risk factors for FMD: model building</td>
</tr>
<tr>
<td></td>
<td>afternoon</td>
<td>All</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2-4 can work with Sergey</td>
</tr>
<tr>
<td>Day 5 Fri</td>
<td>morning</td>
<td>Model building continued</td>
</tr>
<tr>
<td></td>
<td></td>
<td>present to group and discuss interpretation and next steps</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Summary – putting it all together</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Discussion: Next steps</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Feedback from participants about workshop</td>
</tr>
<tr>
<td></td>
<td>afternoon</td>
<td>All</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2-4 can work with Sergey</td>
</tr>
<tr>
<td></td>
<td>Finish by 2 pm</td>
<td>All</td>
</tr>
</tbody>
</table>

5 of 31
**Introduction**

There was a significant FMD type O epidemic in 2010 in both Turkey and Iran, despite extensive vaccination in both countries. The reasons for this epidemic are not fully understood. High meat prices and an associated increase in animal movements regionally are suspected to have played a role. West Eurasia road map for the Progressive Control Pathway aims to lead to the control FMD by 2020. Iran leads epidemiology network in West Eurasian region (consisting of 14 countries) and Turkey, through the SAP Institute, leads the laboratory network.

The Iranian Veterinary Office (IVO) has deployed an extensive data collection system (GIS-VET) across Iran describing all epidemiological units (villages and industrial farms) and containing information on vaccinations applied and FMD clinical disease outbreak reported. With both types of information, certain characteristics are known such as species and type of epidemiological unit involved, location of epi-units, reason for vaccination, number of affected animals in an outbreak etc. Turkey also has collected a wealth of data on FMD outbreaks, vaccination and sero-monitoring activities. These data and their interrelations are of utmost importance to better understand critical components of FMD control. For that reason, swift analysis of these datasets is necessary.

To better understand the analytical value of these data, and to speed up these necessary analyses, there was a need for a one-week get-together of Turkish veterinary and IVO staff and EuFMD epidemiologists. During this week the participants from Iran and Turkey could provide datasets with information on vaccination, outbreaks, laboratory testing and serology for 2010. The workshop provided an opportunity to assist with the analysis of this data with the aim of describing FMD and its control during 2010 and exploring hypotheses behind the upsurge in FMD outbreaks during the year.

During the workshop there was a strong focus on providing training in data analysis and the use of statistical software (Stata, Statacorp, Texas) to the Iranian and Turkish attendants. The workshop also provided the chance to discuss future FMD serological studies in Iran. It is recognised that to control FMD a coordinated regional approach is required. To this end, time was set aside to discuss formats for FMD data sharing between Iran and Turkey; it is hoped that these two countries could lead the way in the West Eurasia region in the sharing of data.

During the EuFMD general session in April 2011, member states will be eager to find out more about the 2010 outbreaks, their occurrence and what effect the control measures had. This information will help with the planning of future control strategies.
Overview of the workshop proceedings

Day 1

Representatives from Turkey and Iran described the data they had brought for analysis.

Dr Rasouli (Iran) described the Iranian data.

There are 356 counties/districts in Iran – all with veterinary services. Reports are made with GPS coordinates to the GIS system – by unit, that is a village (or centroid of) or a large farm, elevation is also record elevation. The units were registered on the system 5 years ago (new units registered as they appear) there are updated when epi-unit visits are made. About 85,000 units exist – of which 56,000 are villages, the rest are various (nomads, water pumps, etc...). Each recorded outbreak is recorded for the unit – this can be mapped visualised via GIS, distance between units, terrain between units etc... can be extracted. This information can easily be extracted to analyse elsewhere (e.g. excel). Interpretations are then based on this outbreak data. This information can be mapped.

Dr Naci Bulut (Turkey) described the Turkish data.

Turkey consists of 81 provinces, each with its own animal health directory. Each province consists of districts (930 in total approx) with many villages. A village is the Epi unit (i.e. the unit of recording), this is defined in legislation. A field veterinarian can define a large farm/feedlot as a unit. Each district has a district veterinary service office (under the control of the provincial directorate). GDPC coordinates the state veterinary services at the national level. In Eastern Turkey livestock management is based on pasture, in the West intensive dairy is more prevalent. Livestock are distributed fairly evenly across the country.

The TURKVET system for is a national database for recording livestock population and disease data. It consists of 3 sections:

1 – Records for large ruminants individually identified with a unique ID (each animal is ear tagged after 20 days); the farmer applies to district veterinary service that then produce a passport for the calf. Small ruminants are recorded by the farm although individual ear tags are applied for small ruminants. Big feedlots record by the farm (uncertainty over this last fact).

2 – Disease recording system

3 – Sample management system (not real-time at the moment). The field veterinarian inputs details on this system, after results obtained from the laboratory, the laboratory loads the results and the field vet can access this data (ready in May 2011).

Vaccinations information is uploaded into Turkvet system at the end of the biannual vaccine campaigns (so not up to date real time).

The morning also included a presentation by Ettore Di Maio on the FAO EMPRES-i information system (http://empres-i.fao.org/empres-i/home) as an example of IT development in animal disease outbreaks and surveillance.
This presentation was set the scene for the data sharing discussions that took place at the workshop. This included structuring and hosting the data (including formatting for data sharing), key IT features, especially web-based features.

The afternoon of the first day commenced with a tour of the SAP institute vaccine production facility.

This was followed by an introduction to stata software, consisting of a presentation by Melissa McLaws and a practical. This practical session focused on loading data into stata and basic data cleaning.

Discussion of the needs and possibilities for data sharing

Discussions were lead by Naci Bulut lead with Naser Rasouli, facilitated by Chris Bartels and Ettore Di Maio.

Participants put forward different information that they thought was necessary and suitable for sharing between Turkey and Iran. The participants from Turkey and Iran and Chris Bartels then indicated which pieces of information should be prioritised for sharing (this is displayed in brackets adjacent to the proposed information to be shared, #1 indicates first priority).

1) Outbreak information with serotyping (Iran #1) (Turkey #4) (Chris Bartels #1)
2) FMD vaccination information (Iran#2) (Turkey #6) (Chris #5)
   a. Which vaccine
   b. Time of vaccination
   c. Coverage by species
3) Genetic analysis results (Iran #5) (Turkey #2) (Chris #3)
4) Vaccine matching results (Iran #3) (Turkey #3) (Chris #2)
5) Important epidemiological events reports (e.g. new serotype, increasing incidence)
   (Iran #1) (Turkey #1) (Chris #1)
6) Serology and serosurvey results (Iran #4) (Turkey #5) (Chris #4)
   a. NSP prevalence
   b. SP antibody surveillance

Naci Bulut stated that genetic analysis is very important to see if the population is likely to be immunologically naive to a particular strain. He also added that blanket vaccination has not been sufficient to protect Turkish livestock from FMD, a major factor in this was the extensive movement of livestock.

Dr Rasouli stated that Iran already send monthly reports to FAO, giving outbreaks by province, and vaccination by province in that month. These reports cover the first points listed above.
Dr Bulut reported that the monthly reports are good but also they would like instant reports of important epidemiological events (so Turkey could step up surveillance and slaughter if a new exotic strain incursion was detected, for example).

The Iranian delegates have found that genetic analysis results from Pirbright take a long time (3-6 months). Naci Bulut reported that at the SAP institute genetic sequence typing takes 15 days to get results. Iran delegates said they are happy to send samples to Turkey. There was a logistical problem with sample transportation between the two countries; however, this was thought to be surmountable. Iranian delegates reported that in order for them to do more diagnostics of their own they would need EuFMD to provide certain reagents.

The discussion on data sharing continued into **day two**. Iran reiterated their willingness to share data. Ettore Di Maio recommended that data be submitted to a central location (e.g. FAO), this would facilitate data sharing in the wider region once more countries participate in the data sharing initiative. Sending raw data that would then be automatically converted into reports and distributed to relevant parties would be the best method, as this allows more flexibility and analysis than if data summaries were sent. Data submission could be done monthly.

Naci Bulut spoke enthusiastically about the initiative but was not in a position to offer data sharing for Turkish data, this would be up to the central vet authorities, whom he will consult.

Dr Rasouli demonstrated the sort of data that Iran could send in an excel table, this included vaccination and outbreak data (written in English), see appendix three for details. Dr Bulut stated that they would be keen to see the Iranian laboratory data too and then briefly described the Turkish data.

The meeting produced a recommendation on data fields to be submitted on a monthly basis to FAO, which will use the Empres-i system to produce an automated monthly report accessible to partners agreed by the project partners (initially Iran, Turkey and FAO). The countries should send a sample of the recommended data to Ettore as soon as possible to produce a sample report for the decision makers to discuss. A summary of the meeting recommendations regarding data sharing are provided in Appendix 7
Day two

After continuing the data sharing discussions (see above), a presentation was given by Theo Knight-Jones on descriptive statistical analysis. The participants continued with practical work on using stata, using Iranian data on vaccination and outbreaks in 2007. This session covered importing data sets, reviewing and cleaning data, do files and basic descriptive analysis. This session continued into the afternoon.

Dr Bulut later gave a talk about sero-surveillance in Anatolia, Turkey 2010.

A two stage sampling strategy was used, sample size was calculated according to 2009 NSP provincial prevalences (at the animal level). Sampled animals were 4-24 months (for small ruminant it was planned to sample up to aged 18 months but actually 24 months maximum age was used due to lack of animals of appropriate age).

Villages were sampled randomly, (1071 villages roughly), sampling 31,000 cattle and 32,000 shoats (sheep and goats). Standard protocols were used to select animals in the villages (e.g. randomly selecting from list of ear tags in the village, but sometimes and crudely selecting animals was used (i.e. non-random)).

Tests performed using the sedi test kit (swanova had a conjugation problem with sheep, but in the future this NSP ELISA kit will also be suitable).

In one year Turkey performs more than 100,000 sero-samples (20-30,000 in Thrace). After questioning Dr Bulut reported that in a study where they vaccinating pregnant cattle and then blood test the calves, after three months of age MDA SP antibodies were not found. It was proposed that such a study be done in Iran.

The value of this serosurveillance was emphasised as in some region they receive no outbreak reports, yet high NSP prevalences are found.

In Thrace, sero-surveys are designed to prove freedom, so sample size calculations are different. NSP positives will occur in FMD free populations, due to imperfect test specificity, these positives need to be followed up to see if they are false positive. Positives are tested on LPB ELISA, titration is also done (?). If positives are clustered it suggests an outbreak rather than random false positives. Follow up investigation includes SP ELISA for serotype.

In Turkey 12% of cattle and 17% of sheep were NSP positive, prevalence is higher in East than West Turkey.

Dr Javad Emami then described a brief serological survey in Iran.

In West Azerbaijan, in over five districts so far, serological sampling was performed on three cows and 13 sheep, all cattle tested NSP positive and as did one sheep. There is concern in Iran that vaccines induce NSP antibodies. Dr Bulut said that disease history information was required, and age of animal; positives should then be tested with LPB. Purified vaccine can also cause false positives particularly if repeatedly vaccinated.
There is a need to record age as repeat vaccination induced false positives and positives in young animals indicate recent infection.

It was suggested that Iran does a field trial, investigating NSP serology in vaccinated animals. A rough outline of this suggested study would be as follows: vaccinate half a village with Razi vaccine and half with Merial vaccine. Later test for NSP serology. If there is not a big difference between the two vaccination groups then wider sero-surveillance would be of use. But it is accepted that Razi vaccine produces NSP response, thus the study may be redundant.
**Day three**

Objectives:
1) Clarification on technical data sharing requirements
2) Further descriptive analysis
3) Design a plan of analysis
4) Demonstration of the Turkvet system??

More practical work was done on using ** stata for descriptive analysis.** Working on a data set of outbreaks and vaccination in Iran in 2010-11 (Persian 1388-89).

-----------------------------------------------------------------------------------------------------------------

**Final summary of data sharing by Ettore Di Maio.**

This clarified which data fields need to be submitted to FAO to produce reports to be distributed to a circulation list. The proposed fields for outbreaks are shown in appendix 7. Further clearance will be requested to permit this data sharing. A prototype report will be produced to show the value of this initiative.

---------------------------------------------------------------

Dr Bulut then gave a demonstration of the Turkvet information system. Each premises has a unique ID, as do all cattle (within 20 days of birth). 60% of small ruminants are identified to the holding. Movements are recorded and updated, vaccination can be recorded as well. Reports can be generated with key statistics. This can be by village, or even individual citizen if required.

Only specific registered people can input data. Sections exist on infectious disease notification, and for different vaccination programmes. Some sort of system has been running since 2000, but there have been many improvements and elaborations since its inception.

To lift quarantine after an FMD outbreak approval of other government bodies are required (date of this approval is recorded). Each notification has a unique number. Laboratory results can be entered by the GDPC on the system and the field veterinarian can see these results. The field veterinarian enters the original data. The field vet then later updates the entry with data on how many visits to the outbreaks there were, when the quarantine was lifted, etc... Generally though the data is entered by the GDPC from paper reports completed and sent by the field vet. As well as the initial and ongoing report sent by the field vet, they also send a final concluding report.

When vaccination is performed the field vet will bring the Turkvet list of animals that should be present and compare it to which animals that are actually present. From this information the Turkvet database is updated. At the Qurban time (religious festival) lots of animals are slaughtered outside official slaughterhouses. The death of these animals is often not updated on the Turkvet system. This is the greatest problem.
Over 500 outbreaks reported this year (2011); reports are received from all over Turkey. This is in part down to increased vigilance due to warnings that were sent out to district veterinarians about the threat of new Afghanistan lineage (with severe signs) and the threat of Asia-1 from Iraq and Iran. More laboratory samples have been than usual as well.

Chris Bartels then led the discussion on forming a plan of future analysis

This considered the following: what data analysis questions are we interested in?
Is risk associated with animal density?
Is risk associated with species?
Outbreak dynamics – how do outbreaks occur in different location over time?
What is the impact of (repeated) vaccination on risk?
What is the age distribution of individuals in outbreaks and how does this affect risk (the required data will have to be assessed)? [But age distribution of animals in epi-units is not recorded]

Age distribution is important for vaccine efficacy. In Turkey if outbreaks also affect the old animals it is thought to indicate that the old multivaccinated animals are not protected and the vaccine has poor efficacy, so they need to have an idea of the age of the cases.

Theo Knight-Jones then made a presentation on vaccine effectiveness, what it is and how to measure it
Javad Emami expressed interest in the idea.
Day 4

Sergei Khomenko introduced himself and gave a brief talk about the recent FMD incursion in Bulgaria where wild boar are suspected to be involved in its spread. It was thought that the role of wild boar in FMD dynamics in Turkey and Iran should be considered. How and where can wild boar surveillance be organised in these regions?

Further practical work was then done on the analysis of the Iran data.

Melissa McLaws and Chris Bartels held discussions with the Iranian group about the EuFMD Iran project and the upcoming mission.

During the week it became apparent that visas would not be available in time for the proposed mission and a new revised date and timetable was made (9-22 April 2011).

Theo Knight-Jones continued with basic stata training and analysis of Turkish data (2010 FMD outbreak, vaccination and denominator data).

It was thought that it would be useful to produce a table showing District code – number of villages – [For types A & O]~ No of outbreaks in year - number of village outbreaks for each month – Incidence per month – Number of livestock/cattle – number of vaccines – average number of doses/animal –

Problems with the Turkish vaccine data meant that this vaccine analysis could not be done during the week.

Naci Bulut then gave a presentation on the 2010 FMD epidemic in Turkey.

FMD Type A (Iran stain??) was less prevalent than type O before 2000. Type A Iran was not covered by vaccination and the population was susceptible, thus it lead to many outbreaks in 2005/6. This FMD A strain circulated for two years but then started to decline. There were two outbreaks of Type O panasia which occurred in 2006/7. After 2007 there was a sharp reduction in outbreaks (600 outbreaks in two years). In 2008 the EC project commenced. It was believed that this project had lead to this reduction (i.e. increased coverage). Animal movements into Turkey were low in 2008/9 thus few animals were imported. Also no new sublineages were discovered in Turkey and the region at that time. Type O SAN09 was detected in Nov 2009, this was thought to be an endemic sublineage, but it turned out to be exotic (unknown origin). It was first located in Sanlofa province (south-east) then by March 2010 it circulated throughout the country. Also found in March 2010 was the new sublineage type O panasia ANT10, detected by the Syrian border, Three months later Pirbright revealed that ANT10 had been circulating in Iran and maybe Pakistan/Afghanistan since 2009. By Sept 2010 this strain was causing many outbreaks throughout Anatolia. Why do they believe it came from the East, perhaps it was first in Eastern Turkey but not detected for some time due to lack of samples submitted from this region. Outbreak investigation may have linked cases on the Iraq border to animal movements from Iraq. By 13th Sept 2010 there had been
947 outbreaks, in the whole year (2010) there had been 1600 type O outbreaks, with a tendency for severe disease and outbreaks in vaccinated animals. GDPC thought more than 85% of the cattle were vaccinated twice a year yet this epidemic still occurred. Dr Bulut believes that after the 2005 Type A Iran outbreak immune immunity levels were high as a consequence of the outbreaks. Vaccine immunity played a lesser role. Post outbreak antibodies last around two years. Also there had not been new sublineages during the inter-epidemic periods (2008/9). When this immunity waned and a novel sublineage incursion occurred it led to severe outbreaks.

Without FMD information from neighbouring countries it makes it hard to be certain of the origin of the sublineage. There is potential for cross border transmission from all the neighbours to the East. Could more have been done if more warning was given of the new lineage in Iran? And how do you identify the emerging sublineages?

In 2010 spring campaign coverage of large ruminants was above 75% for all but three provinces (calculated as number of doses/number of cattle). For small ruminants insufficient vaccine was available for high levels of vaccination (60% coverage, but focus on East and central Anatolia). Seroprevalence tends to be higher in small ruminants as they show few signs so the virus adapts to them, their husbandry conditions also plays a role. A 2007 study in Thrace suggested that there was little transmission from vaccinated large ruminants to unvaccinated small ruminants. But in Anatolia this has not been found to be the case. NSP surveillance is performed in Summer, perhaps seroprevalence would have been much higher if surveillance done in Autumn.

What was Turkey’s response to the outbreaks, its options were mass vaccination, control of movements, outbreak investigations, outbreak measures (ring vaccination, biosecurity, disinfection). Mass vaccination (without booster) is not enough. Better control of movements and quarantine is required. In Turkey field vets incorrectly believe that vaccination will 100% protect. However, incidence risk in many villages was low (perhaps this was due to vaccination). Now more PD 6 vaccine is used but it is not affecting the disease. This is because in an average village 300 out of 1,500 animals are young and only receive one dose in first campaign and are naive until the next campaign). If we focus more on biosecurity and quarantine we can achieve better control, we should not focus on vaccine quality so much.

Does vaccine boost natural immunity?

In Turkey, since Dec 2010 for 3 months there has been an increase due to A Iran 05 Afghanistan07 sublineage (quite different from last year’s lineage of the same name).

Dr Rasouli described the FMD situation in Iran 2010
The upsurge in cases started in March, however, many reported cases in shoats were in fact PPR. The peak was in April with over 1000 shoat and 800 cattle outbreaks. This year and since June 2010 there have been below 200 reports per month and this is tailing off.
An epidemiology curve with vaccinations was produced by Chris Bartels (figure one). This is interpreted by Dr Rasouli as showing increases outbreaks occurring after vaccination, however, this is not at all clear and depends on personal interpretation. We need to consider other factors such as season.

![Epidemiology Curve with Vaccinations](image)

**Figure 1**: FMD vaccination and FMD outbreak reporting for cattle and sheep across Iran between April 2009 and March 2010 (X-axis not yet adapted to Iranian count of dates).

In Iran outbreaks were seen to occur after vaccination. Dr Rasouli believes that for a few days after vaccination animals are immune suppressed. Perhaps vaccine antigen is not inactivated? Introduction of FMD into uninfected units due to poor biosecurity could not be dismissed.

Dr Bulut does not recommend vaccination in outbreak areas (as is done in Iran). If a unit has a dangerous contact then do not vaccinate.

Vaccination was conducted 19 Sept 2010 to 22 Oct 2010. (23,420 villages in this time), 32,226 were not vaccinated. Outbreaks were investigated 26 Oct 2010 to 15 Dec 2010. Outbreaks in the two “cohorts” were assessed. For vaccinated villages 158/23,262=0.0067 experienced outbreaks, for vaccinated villages 49/34226=0.0014 experienced outbreaks, relative risk= 4.78. This was taken from all the villages vaccinated in the country (approx 56,000 villages in total). Biases obviously exist (e.g. selection of farms to vaccinate, ascertainment). Changes to policy as a result are: after an outbreak a protection zone is created around an outbreak within which vaccination was practiced. Now after outbreaks they try to discourage people entering the protection zone but do not perform ring vaccination (nationwide).
A map of the 2010 outbreaks was produced, however, the importance of relating outbreaks to the denominator is very important and was not shown.
Day 5

Discussions were made on the serological studies proposed in the Iran mission report “Combating Foot and Mouth Disease through enhanced and coordinated surveillance activities: Phase III of the FMD surveillance centre initiative” by Chris Bartels.

There was disagreement on some of the terminology of the descriptions (this was emphasised by the virology experts present). It was reported that apparently Razi vaccines already do some potency tests but this needs clarifying.

The proposed SP testing needs more thought as is difficult to test and interpret with the many vaccine serotypes.

For study 2 – Dr Rasouli reported that dairy farms keep individual vaccine records (this could be useful for other field studies that may be undertaken in the future).

Dr Bulut advised not to exclude beef farms from sero-surveys (as in one of the proposed studies). He stated that you may struggle to get sufficient sample size in certain age-groups in certain village settings. In Turkey villages the average number of cows per farm is seven with 300 per village.

It was concluded that the proposals needed clarifying, e.g. by putting in a table with more diagrams. It was agreed that EuFMD would do this and send the revised proposals to Dr Bulut and Dr Rasouli.

---------------------------------------------
Sergi Khomenko discussed GIS analysis options available to the countries.

All epi-units in Iran have geographical coordinates and much GIS work is already done. In Turkey coordinates were missing for many villages (40%??). In addition shape files were not immediately available for Turkish districts and provinces. This problem was to be investigated after the workshop.

The benefits of considering dominator data and geographical density were explained for such spatial analysis.

For the end of the workshop - focal contacts were specified for follow up work relating to the workshop. They are:
For Turkey – Sibel Gungordu at GDPC and Naci Bulut at SAP
For Iran - Dr Sholehpash.

The need for future technical assistance in Turkey was to be discussed with Haluk at GDPC, Dr Bulut was enthusiastic about the idea. It was believed by the attendants that the information produced by the sorts of analysis that was done and discussed during the week would be useful for managers.
The participants were given Stata “homework” exercises and encouraged to contact the trainers with any questions that arise.
Appendix 1: List of workshop attendants.

From EuFMD

Dr Melissa McLaws - Consultant veterinary epidemiologist, EuFMD  
melissa.mcLaws@fao.org

Dr Chris Bartels – Consultant veterinary epidemiologist, EuFMD  
c.bartels@gddeventer.com

Ettore De Maio – Datasystems expert, GLEWS project, FAO  
Ettore.Demaio@fao.org

Sergei Khomenko – Expert in wildlife diseases and GIS, FAO.  
sergei.khomenko@fao.org

Theo Knight Jones - Consultant veterinary epidemiologist, EuFMD  
tkjones@rvc.ac.uk

From Iran

1 - NASER RASOULI BEIRAMI, VETERINARY OFFICE FOR SURVEILLANCE OF  
LIVESTOCK DISEASES (IVO headquarters)  
beirami40@hotmail.com

2 - MOHAMMADREZA SHOLEHPASH, VETERINARY OFFICER FOR SURVEILLANCE  
OF LIVESTOCK DISEASES. (IVO headquarter)  
dr_sholehpash@yahoo.com

3 - JAVAD EMAMI, VETERINARY OFFICER FOR SURVEILLANCE OF ANIMAL  
DISEASES (West Azerbaijan province)

4 - SEYED ALI EMAMI, VETERINARY OFFICER FOR SURVEILLANCE OF  
LIVESTOCK DISEASES, (Tehran province)  
dr.emami.ali@gmail.com

From Turkey

Dr Naci Bulut - Coordinator of sero-surveillance, EuFMD standing technical committee,  
Head of diagnostics, Sap institute, Ankara, Turkey  
nacib@sap.gov.tr

Dr Sibel Gungordu – PhD Microbiology, GDPC, Ankara, Turkey,  
sgungordu@hotmail.com

Dr Can Cokcaliskan – PhD Virology, Serology dept., Sap institute, Ankara, Turkey  
cancokcaliskan@gmail.com
Appendix 2: Data recorded in Iranian GIS vet system for outbreaks.

Unit name
Unit ID
Unit type
  Epi unit code
  1 – shoat
  2 – beef farm
  3 – dairy farm
  8 – pastures (nomad)
  9 – village

Disease detected
Disease code
Has vaccination be carried out
When did vaccination occur
Who reported the outbreak
Code for who reported outbreak
(New page in information form):
  What kind of animal species in outbreak (cow/sheep/goat/mixed...)
  Which age of animals were affected (categories)
  Number of animals in outbreak (sometimes put number of animals/sometimes number checked)
  How many animals affected
  How many died
  How many animals checked
  How many animals vaccinated
  How many culled (should be zero)
  Details of animals entering units (e.g. purchase)
*examination of outbreak not done by fixed protocol e.g. selection of animals to be examined not fixed
Clinical Symptoms
PM pathology detected
New page for lab results
Outbreak code
Sample type
Number of samples
Who took the samples
Date of sampling
Date sample sent
Which laboratory used
Date of results
What diseases detected

Another sub-table exists to record vaccination – this includes, date, unit code (etc...), number of animals

Appendix 4: Coding of Turkish laboratory test data.

Turkey laboratory database
Species:
BUZA?I = calf
CEYLAN =
DOMUZ = pig
KEÇ? = goat
KOYUN = sheep
KUZU = lamb
MANDA =
O?LAK = kid
SI?IR = cattle

KE4? = goat
Koyun = sheep
Hols = Holstein
Bo? = missing data
Kegi = goat
S???r = cattle
S???R = cattle

Final result:
+ = pcr positive but not typed
??LEM = result pending
?MHA = destroyed sample
A = A
NEGAT?F = negative
O = O
POZ?F = probably positive but not typed

Appendix 5: Original proposal for validation and analysis of Turkish and Iranian (GIS-VET) FMD data

By Dr. Chris J.M. Bartels, backstopping officer
Melissa McLaws, supervisory officer
14 January 2011

To the attention of Dr Keith Sumption, secretary EU-FMD commission, FAO, Rome, Italy

Introduction

There was a significant FMD type O epidemic in 2010 in both Turkey and Iran, despite extensive vaccination in both countries. The reason for this epidemic are not fully understood as yet, but high meat prices and an associated increase in animal movements regionally are suspected to be involved.

The Iranian Veterinary Office (IVO) has deployed an extensive data collection system (GIS-VET) across Iran describing all epidemiological units (villages and industrial farms) and containing information on vaccinations applied and FMD clinical disease outbreak reported. With both types of information, certain characteristics are known such as species and type of epidemiological unit involved, location of epi-units, reason for vaccination, number of affected animals in an outbreak etc. Turkey also has collected a wealth of data on FMD outbreaks, vaccination and seromonitoring activities. These data and their interrelations are of utmost importance to better understand critical components of FMD control. For that reason, swift analysis of these datasets is necessary.
To better understand the analytical value of these data, and to speed up these necessary analyses, there is a need for a one-week get-together of Turkish veterinary and IVO staff and EuFMD epidemiologists.

**Objective**
During a one-week meeting, two staff from each of the Turkish Veterinary Services and IVO sit together with EuFMD epidemiologists to validate the available data from Turkey and Iran, to define and perform descriptive and statistical data-analyses to better understand the current upsurge of FMD outbreaks. Including veterinarians from both countries will allow for a regional, as well as national, perspective to the analysis. They will also develop a plan for the continuation of these analyses in this year, 2011.

This meeting will also provide training for the Iranian and Turkish staff in data analysis and use of statistical software.

**Method**
This meeting will combine training on data-exploration with statistical data-analysis such that upon return Turkish and IVO staff can continue to work on the planned analyses.

It is proposed to have two Turkish and IVO staff involved as this will lower the burden placed on a single person, it will speed up the necessary data analysis and they can act one another's back up after the meeting.

For data validation and data analysis, training will be provided using a trial version of STATA 11. The training will be conducted in English.

**Results**
The outcome of this meeting will include the following *(note: proposed analyses are based on available Iranian data, analyses may be modified for Turkey depending on the nature of the available data)*

- Description of vaccination coverage between 2006 and 2010, with stratification by species (large versus small ruminants), type of epidemiological units (industrial versus village), type of vaccination (emergency versus routine) and province/districts.
- Description of clinical and laboratory confirmed FMD outbreak reports between 2006 and 2010, for all provinces with stratification by species (large versus small ruminants), type of epidemiological units (industrial versus village), virus type (A, O), type of vaccination (emergency versus routine) and province/districts.
- Interrelation between vaccination and FMD outbreak reporting to determine possible determinants for FMD outbreaks
  - What are putative risk factors for FMD outbreak reporting? What is the relevance of vaccinating small ruminants in villages? By what percentage is the probability for a FMD outbreak reduced when epi-units are vaccinated more often?
  - Are there effects over time? Does the risk of an FMD outbreak change over time for certain species, certain locations, certain epi-unit types?
- For all analyses, inclusion of population data *(total number of animals, total number and location of epidemiological units)* is essential.

In the next mission to Iran (April 2011), results will be used to continue discussions on the FMD control strategy with the FMD task force.

**Necessary data to bring along:**

I) Population dataset - list of epi-units and number/species of animals

With variables: 0. Epi-unit code (numerical), 1 Province (Latin script), 2 District (Latin script), 3 Village, name or name of industrial farm (Latin script), 4 Epi unit type – categories, 5 Number of cattle – numerical, 6 Number of sheep – numerical, 7 Number of goats – numerical, 8 X-Y coordinates of district centroid (may be given in a separate dataset), 13? Distance to nearest city? (more than 100,000 people?) 14 Distance to nearest live animal market?

II) Vaccination dataset
With variables: 0 Epi-unit code (numerical), 9 Date of vaccinations (2007-2010), 1 row for each date of vaccination, 9a. date of vaccination, 9b. species vaccinated, 9c. # animals vaccinated, 16 reason of vaccination.

III) Surveillance dataset

With variables 0 Epi-unit code (numerical), 10 Date of surveillance visits (2007-2010), 11 result of surveillance (i.e. outbreak yes or no) (categorical), IV) Outbreak dataset, these data are already provided, 0. Epi-unit code (numerical), 12 Date of outbreaks (2007-2010), 15. species affected, 15b number of animals affected, 15c number of animals dead, 16 outbreak found by 1) active or 2) passive surveillance (categorical).

Planning
This training will be provided at the FAO office in Ankara, Turkey. The proposed dates are March 13-17, 2011.

<table>
<thead>
<tr>
<th>Day</th>
<th>Data analysis activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>Introduction: datasets and software</td>
</tr>
<tr>
<td>Day 2</td>
<td>Data cleaning and descriptive analysis</td>
</tr>
<tr>
<td>Day 3</td>
<td>Descriptive analyses continued, introduction to regression modelling</td>
</tr>
<tr>
<td>Day 4</td>
<td>Multivariable analysis to determine risk factors for FMD: model building</td>
</tr>
<tr>
<td>Day 5</td>
<td>Multivariable analysis continued (model checking)</td>
</tr>
</tbody>
</table>

Appendix 6: Initial draft Iranian data analysis from the week (Chris Bartels)

Data set of FMD vaccinations and reported FMD outbreaks in Iran between April 2009 and March 2010

Population data based on census data collected when the GIS-VET system was established in 2005

- In Iran there are 85117 registered epiunits, 67.2% villages, 13.6% dairy farms and 18.7% other farm types or units (waterpump, pastures etc).
- A total of 8.00 million cattle were recorded and 81.6 million sheep (and goats) at this time.

Vaccination data between April 2009 and March 2010

- 261787 recorded vaccination events
- A total of 44.9 million cattle and sheep were vaccinated in 2009 and 23% more in 2010.
- Within epi units, the vaccination coverage was 92% or higher, regardless epi unit type and species
- However, related to the number of animals counted in 2005, the vaccination coverage in 2010 was between 148% and 279% for cattle (where the policy is to vaccinate 3 times a year, equalling 300%) and was between 47 and 153 for sheep (where the policy is to vaccinated once a year, equalling 100%)
- Best vaccination performance is seen on dairy farms and least in other types.

<table>
<thead>
<tr>
<th>Species</th>
<th>Epi unit type</th>
<th>2009</th>
<th>2010</th>
<th>Census*</th>
<th>% vaccination related to 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle</td>
<td>Village</td>
<td>9219805</td>
<td>9467772</td>
<td>6393270</td>
<td>148</td>
</tr>
<tr>
<td></td>
<td></td>
<td>92.0%</td>
<td>95.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dairy farms</td>
<td>1773836</td>
<td>2428711</td>
<td>870784</td>
<td>279</td>
</tr>
<tr>
<td></td>
<td></td>
<td>95.3%</td>
<td>95.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>1010076</td>
<td>1182623</td>
<td>744442</td>
<td>159</td>
</tr>
<tr>
<td></td>
<td></td>
<td>93.5%</td>
<td>95.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sheep</td>
<td>Village</td>
<td>27.7 million</td>
<td>34.7 million</td>
<td>66.0 million</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td></td>
<td>94.0%</td>
<td>95.1%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Based on epi units, the percentage of epi units vaccinated over time differs between 52.0% in 2009 and 61.3% in 2010.

- Villages are most frequent vaccinated and 'other epi units' are least vaccinated.

### Epi Unit Type

<table>
<thead>
<tr>
<th>Epi Unit Type</th>
<th>Vaccinated in 2009</th>
<th>Vaccinated in 2010</th>
<th>Census* Related to 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Village</td>
<td>35365</td>
<td>38897</td>
<td>57645</td>
</tr>
<tr>
<td>Dairy farms</td>
<td>5320</td>
<td>7196</td>
<td>11545</td>
</tr>
<tr>
<td>Other</td>
<td>4614</td>
<td>6088</td>
<td>15927</td>
</tr>
<tr>
<td>Total</td>
<td>45299</td>
<td>52181</td>
<td>87115</td>
</tr>
</tbody>
</table>

* as recorded at the start of GIS-VET in 2005

- in more detail, in the following table, the frequency of vaccination per year is given
- Overall, the vaccination performance in 2010 is higher than in 2009
- For villages, 2/3 of villages have been vaccinated at least once in 2010, however only 35.7% were vaccinated three times.
  - For dairy farms this was slightly less
  - However for other epi units, the percentage of units vaccinated was 38.2% once and only 11.8% three times in 2010

### Outbreak Data

- FMD reported outbreaks between April 2009 and March 2010
  - 7883 outbreaks
  - 56.5% in cattle and 43.5% in sheep, with great difference between years: in 2009 the percentage of outbreaks in sheep was 32.7% and in 2010 48.8%
  - 82.1% in villages, 6.5% in dairy farms and 11.5% in other farms/units with no differences between years
FMD vaccination and FMD outbreak reporting for cattle and sheep across Iran between April 2009 and March 2010 (X-axis not yet adapted to Iranian count of dates).
Vaccination and outbreak reporting for villages across Iran between April 2009 and March 2010 (X-axis not yet adapted to Iranian count of dates).

![Graph showing vaccination and outbreak reporting for villages across Iran between April 2009 and March 2010.]

Vaccination and outbreak reporting for dairy farms across Iran between April 2009 and March 2010 (X-axis not yet adapted to Iranian count of dates).

![Graph showing vaccination and outbreak reporting for dairy farms across Iran between April 2009 and March 2010.]

Legend:
- Reported FMD outbreaks
- Recorded FMD vaccinations
- (sum) outbreak
- (sum) vac
Vaccination and outbreak reporting for epi units other than villages and dairy farms across Iran between April 2009 and March 2010 (X-axis not yet adapted to Iranian count of dates).

**Relation between FMD vaccination and FMD outbreak reporting**

An example, epi unit 10010118, a village in Behbehon district in Khuzestan province.

First recorded vaccination is on 05 May 2009, 187 cattle out of 187. 126 days later, again cattle are vaccinated (325 out of 325). Then on 8 November, an FMD outbreak reported in sheep (31 clinical out of 239 susceptibles). A day later, sheep are vaccinated (300 in total). A week later (16 Nov), FMD outbreak in cattle (1 clinical out of 300 susceptible) and the next day 300 cattle vaccinated.

59 days after the outbreak vaccination in sheep, 285 sheep are vaccinated and 20 days later 196 cattle are vaccinated. Later in May, 290 sheep are vaccinated but no cattle and in October 350 sheep and 260 cattle are vaccinated.

Table. Example of FMD vaccination and FMD outbreak reporting in a single epiunit (village) for cattle and sheep in that village.

<table>
<thead>
<tr>
<th>Cattle</th>
<th>Days between</th>
<th>Vx</th>
<th>126</th>
<th>Vx</th>
<th>69</th>
<th>FMD</th>
<th>Vx</th>
<th>71</th>
<th>Vx</th>
<th>251</th>
<th>Vx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timeline</td>
<td>05/05</td>
<td>08/09</td>
<td>08/11</td>
<td>09/11</td>
<td>16/11</td>
<td>17/11</td>
<td>07/01</td>
<td>27/01</td>
<td>19/05</td>
<td>05/10</td>
<td></td>
</tr>
<tr>
<td>Days between Sheep</td>
<td>-</td>
<td>59</td>
<td>→</td>
<td></td>
<td>132</td>
<td>→</td>
<td>139</td>
<td>→</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FMD</td>
<td>Vx</td>
<td>→</td>
<td></td>
<td></td>
<td>Vx</td>
<td>→</td>
<td></td>
<td></td>
<td>Vx</td>
<td>→</td>
<td>Vx</td>
</tr>
</tbody>
</table>
Appendix 7: Data Sharing: meeting recommendation
Developed in Ankara, 14-18 March 2011

1. Considering that: the 2010 West Eurasia roadmap meeting held in Istanbul in December 2010 recommended greater sharing of information regarding FMD with the overall aim to improve early warning of new regional threats/epidemics,

2. The meeting recommends that
   a. Iran and Turkey send data on FMD outbreaks and vaccination on a monthly basis to FAO Empres-i
   b. Data will be collected by using Excel files or “Comma Separated Values” files
   c. FMD outbreak data will include (mandatory fields are underlined):
      i. ID
      ii. Province
      iii. District
      iv. Latitude
      v. Longitude
      vi. Elevation
      vii. Locality Name
      viii. Reporting Date
      ix. Observation Date
      x. **Cattle Susceptible**
      xi. **Cattle cases**
      xii. Cattle Loss
      xiii. Cattle Death
      xiv. Cattle Stamping out
      xv. **Small ruminants Susceptible**
      xvi. **Small ruminants cases**
      xvii. Small ruminants Loss
      xviii. Small ruminants Death
      xix. Small ruminants Culled
      xx. Species Tested
      xxi. Test Method
      xxii. Sample Type
      xxiii. Laboratory Name
      xxiv. Test Date
      xxv. Result
      xxvi. Vaccine matching result
      xxvii. Genetic analysis result

      (** at least one between Cattle/Small ruminant has to be filled)
d. Vaccination data will include (mandatory fields are underlined):
   i. **ID**
   ii. **Province**
   iii. **District**
   iv. **Latitude**
   v. **Longitude**
   vi. **Elevation**
   vii. **Locality Name**
   viii. **Type of Vaccine**
   ix. **Vaccination Date**
   x. **Cattle Population**
   xi. **Cattle Vaccinated**
   xii. **Small ruminants Population**
   xiii. **Small ruminants Vaccinated**

   (**at least one between Cattle/Small ruminant has to be filled)**

e. It has been pointed that longitude and latitude have to be used only for “internal purposes” (to EuFMD and FAO HQ): when providing to a public audience outputs coming from the data (both in public web interfaces and when producing documents/files), the Locality Name has to be displayed and, when a map has to explain where the event occurred, the District’s Centroid has to be used instead of precise coordinates.

f. The System which collect the data will provide the possibility to produce reports to output analytical results. Reports will be made thanks to Templates with empty grids and charts, to be filled “on demand” with real data.
   i. The monthly epidemiological report currently submitted to EuFMD by IVO has been assumed as a pilot to start, for all the sections for which data are provided in the abovementioned lists of fields.

\[31\] of \[31\]

\[31\] of \[31\]

\[31\] of \[31\]