Animal Health Surveillance in the context of Genetically Modified feed.

Louise Vince (The Royal Veterinary College, University of London)
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Development of an epidemiological model to assess the ability of different monitoring strategies to identify potential adverse outcomes which could be attributable to GM feed.

Impact: Such a model could be used to inform future monitoring of the health effects of GM-crop derived animal feed in livestock; it could form the basis of scientific approaches towards the identification of potential linkages between animal health and GMO consumption.
GM feed undergoes rigorous pre-market testing in the EU allowing for good consumer confidence in both animal and human health of products.

Allergenicity, Toxicity, Nutritional effects, Horizontal gene transfer and other environmental safety concerns are addressed and considered in depth.
Literature on adverse health effects on the whole agrees with the overall safety of the permitted varieties.

90 day feeding trails in rodents and some livestock.

A few longer term studies are available which agree with the safety of GM feed.

No consistent evidence exists to indicate specific risks.
Feed is both grown in the EU and imported from outside the EU. Traceability of feed being used on a given livestock population is extremely challenging.

- Currently 62 different variants are grown with more imported.
- Consumption is highly price variable.
- The degree of uncertainty and variability precludes any useful ‘exposure’ measurement at this stage.
Objectives of Model Outputs

To evaluate at population level the possibility that if adverse events occurred what would be the sensitivity of detection of:

1) Changes to production variables as a result of GM Variants.

2) Adverse effect on known current disease states.

3) Unknown and unforeseen adverse effects.

The breadth of these requirements required a flexible dynamic model, with a wide applicability.

The model can assess the ability to detect, can inform the best strategy to detect, can identify the “problems” that are more likely to be detected.
PURPOSES OF SURVEILLANCE

Before considering how to best implement animal disease surveillance, we should first have a clear understanding of why we need to do surveillance. There is a large number of reasons why veterinary authorities undertake surveillance activities, but these can be summarised into four general purposes:

Demonstrating freedom from disease
Early detection of disease
Measuring the level of disease
Finding cases of disease
Case Detection

Purpose: Adverse event reporting.

Reporting by the farmer and local vet to a regulatory body.

Requires:
• Identification / Detection of an abnormality.
Framework of the Model

Applies tools from syndromic surveillance.
Does not depend upon quantification of ‘exposure’.

Requires specification of animal subpopulations (species, system)

Output: likelihood that a certain monitoring effort detects selected animal health outcomes in selected subpopulations
Defining Syndrome Variables

Standard Body Systems used for syndromic surveillance

Standardised with UK and European systems

Reproduction (Abortion)
Reproduction (fertility)
Eyes, Ears and Integument
Musculoskeletal
Cardiovascular
Neurological
Gastro-Intestinal
Respiratory
Systemic
Mastitis
Treatment Failure
Sudden Death / Fallen Stock.
<table>
<thead>
<tr>
<th>Model Structure</th>
</tr>
</thead>
</table>

**Integration of Surveillance Components**

- Passive On farm Surveillance
- Industry Data
- Abattoir Surveillance
- Post Mortem Findings
- Active Government - Level Surveillance
Types of Surveillance

Animal Health surveillance occurs across the EU for may reasons.

- Monitoring of endemic disease (Prevalence studies).
- Proof of disease freedom and international reporting. (Notifiable Infectious Disease).
- Industry Monitoring.

- To date little surveillance has been orientated around feed related risks.
Probabilistic scenario tree modelling – Passive Surveillance

Risk Group - Diary Cattle.

- P. Clinical Signs are Present
  - P. Farmer Detects Clinical Signs.
  - P. Clinical signs are not detected.
- P. Clinical Signs are Absent.
  - P. Local Vet collects Samples
    - P. Samples Tested positive
    - P. No Disease diagnosed.
  - P. Local Vet does not collect samples
    - P. Local Vet is not called.
# Component 1 – Farm Level Passive

## Farm Level - Sensitivity of detection (Passive System)

<table>
<thead>
<tr>
<th>Risk Syndrome 'Sign'</th>
<th>Probability of Event Occurring</th>
<th>Clinical Signs Observed by Farmer</th>
<th>Local Vet Called</th>
<th>Samples taken</th>
<th>Test positive for 'known' etiology.</th>
<th>Outcome</th>
<th>Prob</th>
<th>Check sum</th>
<th>Unit se</th>
<th>Overall Sensitivity</th>
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</tbody>
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**Input Data**  
- Repro (Abortion)  
- Repro (Fert)  
- Eyes, Ears & Integument  
- Systemic  
- GIT  
- RES ...  

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**Table Columns:**  
- Risk Syndrome 'Sign'  
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- Local Vet Called  
- Samples taken  
- Test positive for 'known' etiology.  
- Outcome  
- Prob  
- Check sum  
- Unit se  
- Overall Sensitivity
Each surveillance component requires parametrisation with data. These can include:

- Expert opinion data,
- Published data from literature,
- Specific detailed surveillance data.
Combining components

<table>
<thead>
<tr>
<th>Population, Farm Level Simulation</th>
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<tbody>
<tr>
<td>Number of Iterations</td>
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<td>Relative Risk</td>
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<td>GM Exposure Component</td>
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<table>
<thead>
<tr>
<th>Multi-Herd Model</th>
<th>Baseline Detection rates</th>
<th>Exposed Detection rates</th>
<th>Combined Probability of</th>
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<tr>
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</table>

<table>
<thead>
<tr>
<th>Multi-Herd Model</th>
<th>Simulation Baseline No. of Farms Affected</th>
<th>Simulation Exposed No. of Farms</th>
<th>P Value of a difference (Chi</th>
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<tr>
<td>CVS</td>
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<td>646</td>
<td>262</td>
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</table>
Example of Component contribution to overall sensitivities

Combined_Sens_REP...
Inputs Ranked By Effect on Output M...

REP(A) / Industry Monitoring: 0.13405, 0.55107
REP(A) / Abattoir Detection: 0.21669, 0.46989
REP(A) / On Farm Detection: 0.25079, 0.43528
REP(A) / National Surveillance: 0.25481, 0.41538
REP(A) / Post-Motem: 0.24658, 0.39674

Baseline = 0.32898
Methods

- Probabilistic modelling using excel and @risk 6.3 was performed to identify detection rates for disease syndromes.
- Mathematical simulations were run to establish if, in the event of GM feed causing an increase in the prevalence of a certain endemic syndrome, the increase would be detectable by the surveillance systems in place.
- Monte Carlo sampling was used to perform stochastic simulation of both endemic and unknown conditions.
Probability of detecting a change of 5% based on passive surveillance in the UK with 95% Confidence.
• Sensitivity of detecting a change varies with syndrome.
• Doesn’t appear to be related with the prevalence of the underlying condition.
• Based on UK data No syndrome has the ability to accurately detect a change of at least 5% in endemic or existing ‘syndromes’ with a certainty greater than 80%.
Probability of detecting a change in the UK Integumentary system in the UK
The Integumentary system represents a higher sensitivity syndrome in the UK.

The probability of detecting a change of at least 1% above the baseline is 50%.

The Probability of detecting a change of at least 20% increases to 80%.
Probability of detecting a change in Neurological conditions at different changes in prevalence with 95% Confidence in the UK

Magnitude of Change in Prevalence vs. Probability of detecting a change in Neurological Conditions.
• The Neurological system represents a disease system which has a low sensitivity of detecting a change.

• The probability of detecting an increase of 1% in existing conditions at is 1%.

• The probability of detecting an increase of 20% is 3% at farm level.
Sensitivity of the surveillance system for feed related syndromes detectable in Spain

Probability of detecting a change of at least 5% in a diary population (model parameterized based on values from Spain.)
• EU wide surveillance programs exist for infectious disease monitoring but less so for endemic disease.
• Sensitivity of detection of changes due to GM feed are currently insufficient to detect a change with any degree of certainty.
• Increasing the sensitivity of detection may be possible with targeted reporting.
• Specificity increase and multi-variate monitoring may help to improve case definition.
Project Partners

Stichting Dienst Landbouwkundig Onderzoek
WEBSITE: www.rikilt.wur.nl/uk

AgrobioInstitut (Agrobioinstitute - ABI)
Website: www.abi.bg/index.php?lang=en/

Freie Universität Berlin (FUB)
Website: www.fu-berlin.de/en

Institut National de la Recherche Agronomique (INRA)
Website: www.international.inra.fr

Institut de Recerca i Tecnologia Agroalimentaries (IRTA)
Website: www.irta.cat/en-US

Istituto Superiore di Sanita (ISS)
Website: www.iss.it/

The Royal Veterinary College (RVC)
Website: www.rvc.ac.uk/

Sociedade Portuguesa de Inovação (SPI)
Website: www.spieurope.eu

Università degli Studi di Camerino (SVMS)
Website: www.unicam.it/

Universitat de Girona (UdG)
Website: www.udg.edu/

Università degli Studi della Tuscia (UNITUS)
Website: www.unitus.it