PARASITOLOGY IN 2020
Where will we stand?

EU Framework Programmes
PARASOL & GLOWORM & PARAVAC
All grazing ruminants are infected with helminths, however, only some need to be treated.
## Production diseases

<table>
<thead>
<tr>
<th>Disease Name</th>
<th>Score</th>
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</thead>
<tbody>
<tr>
<td>Coccidiosis</td>
<td>226.20</td>
</tr>
<tr>
<td>Paratuberculosis</td>
<td>222.81</td>
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<tr>
<td>Liver Fluke</td>
<td>201.98</td>
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<tr>
<td>Nematodes</td>
<td>192.85</td>
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<tr>
<td>PCV II</td>
<td>182.67</td>
</tr>
<tr>
<td>BVDV</td>
<td>182.45</td>
</tr>
<tr>
<td>Small ruminant mastitis</td>
<td>179.11</td>
</tr>
<tr>
<td>Varroa mite</td>
<td>176.61</td>
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<tr>
<td>Staphylococcus aureus mastitis</td>
<td>174.92</td>
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<tr>
<td>Theileria</td>
<td>173.71</td>
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<tr>
<td>Mycoplasma Bovis</td>
<td>173.27</td>
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<tr>
<td>Swine Influenza Virus</td>
<td>162.41</td>
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<tr>
<td>Swine A. pleuropneumonia</td>
<td>159.13</td>
</tr>
<tr>
<td>BRSV</td>
<td>153.29</td>
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<tr>
<td>Swine Mycoplasma</td>
<td>142.47</td>
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<tr>
<td>BHV-I (IBR)</td>
<td>106.66</td>
</tr>
<tr>
<td>PRRS</td>
<td>106.65</td>
</tr>
<tr>
<td>Environmental/ Strept mastitis</td>
<td>82.48</td>
</tr>
</tbody>
</table>
Economic importance of helminth infections in the EU (€ millions)

Anthelmintic drugs in EU: € 400 million / year

<table>
<thead>
<tr>
<th></th>
<th>Dairy Cattle</th>
<th>Beef</th>
<th>Sheep</th>
<th>Others</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>Fasciolosis</td>
<td>700-1200</td>
<td>200-400</td>
<td>150-300</td>
<td>&gt;50</td>
<td>1100-2000</td>
</tr>
<tr>
<td>Nematodes</td>
<td>1000-1500</td>
<td>400-800</td>
<td>300-400</td>
<td>&gt;100</td>
<td>1700-2800</td>
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</table>
Sharp increases in helminth-associated disease frequency and intensity have been reported within the European ruminant sector in recent years

Why?

➡️ Global changes: e.g. farm management, climate and decreased efficacy of anthelmintics (AR)
➡️ Currently no alternatives for anthelmintics e.g. vaccines
The Evolution of Veterinary Medicine

Clinical disease

Subclinical disease

Performance targets

Observation

Diagnostics

Data

Treatment

Prevention

Advice

Animals

Records

People

Adapted from: LeBlanc et al, J.Dairy.Sci. 2006
Implementation of novel solutions for helminth infections in ruminants

Needs

Solutions
FP6 & FP7

Implementation
Horizon 2020
We need **monitoring tools** that:

1. Are affordable, easy to interpret, practical for large scale use

2. Values reflect nematode-induced production losses ( = financial effects)

3. Allow recommendation of appropriate preventive measures
We need control tools that prevent production loss. We need to shift from maximal to optimal parasite control.
To control helminth infections:

① At present efficient control relies almost exclusively on effective anthelmintic drugs.

② The increasing occurrence of anthelmintic resistance (AR) in worm populations threatens the efficiency of livestock production.

③ So we should use anthelmintics **ONLY** when necessary **AND** we need other control tools e.g. vaccines.
Implementation of novel solutions for helminth infections in ruminants

- Needs
- Solutions FP6 & FP7
- Implementation Horizon 2020
FP6 & FP7 Projects

- **PARASOL** - Novel solutions for the sustainable control of nematode ruminants
- **GLOWORM** - Innovative and sustainable strategies to mitigate the impact of global change on helminth infections in ruminants
- **PARAVAC** - Vaccines against helminth infections
- **DELIVER** - Control of fasciolosis
What was Parasol?
- FP6 project, 2006 – 2009, budget 3 million €
- Coordinator – Jozef Vercruysse (Ghent University)

Why Parasol? Current strategies are not sustainable:
- Treatments are usually given without enough supporting diagnostic or epidemiological information
- Frequent/suppressive whole flock/herd treatments
- Reduced efficacy of current and new compounds
Innovative PARASOL strategies

- Targeted treatments (TT) given to the entire flock/herd according to diagnostic information
- Targeted selective treatments (TST) are those where individuals within the group are treated on the basis of need

To reduce the unnecessary use of anthelmintics will consequently:

- Minimise residues in food and the environment
- Provide a parasite population in *refugia*
- Delay emergence of AR
We showed that

- TT & TST strategies work
- Parasitological/performance criteria can be used

The performance/parasitological criteria to be used will be regionally variable and different between livestock species.

These approaches are also economically competitive
Key findings (2)

- Small ruminants treatment indicators e.g.
  - Weight gain, milk production
  - Anaemia (FAMACHA), diarrhoea scoring
  - Faecal egg counts

- Cattle treatment indicators e.g.
  - *Ostertagia* and *Fasciola* milk ELISA at housing
  - Serum pepsinogen testing at housing
  - Mid season FEC and weight gain?
Implications and recommendations

- The introduction of TT/TST strategies to worm control will require the active co-operation of veterinarians, agricultural advisory services, farmers and the animal health industry.

- Need for automation/decision support systems to encourage uptake of TT/TST strategies by farmers.

- They should be actively promoted to enable effective and sustainable worm control in ruminants.
What is Gloworm?

- FP7 project, 2012 – 2014, 3 million €
- Coordinator – Jozef Vercruysse (Ghent University)

Why Gloworm?

- Changes in climate, environment and livestock farming have an impact on the epidemiology, seasonality and geographic distribution of helminth infections.
- Sustainable control of helminth infections in a changing world requires detailed knowledge of these interactions.
Association network illustrating how **global changes** may influence pasture contamination with helminths.

**Global changes**
- Climate
- Land use
- Husbandry
- Farm income
- Farming intensification

**Parasite contamination**
- Diseased animals, reduced productivity
- Increased anthelmintic resistance
- Increased reliance on anthelmintics

**GLOWORM**
Horizon 2020
Horizon 2020

**DIAGNOSTICS**
- High throughput, quantitative
- Multiple parasite species
- Economic thresholds
- Anthelmintic resistance

**MODELS, RISK MAPS**
- Spatial & temporal distribution
- Forecasting infection risks

**GLOWORM strategy**

**AUTOMATED DECISION SUPPORT** for end-user

**GLOBAL CHANGES**
- Climate
- Land use
- Farm management

**TREATMENT**
- When? (TT)
- Which animals? (TST)

Financial return
New diagnostic tools for simultaneous/multiplex detection of parasite species

- Liver fluke
- Lungworm

Optimized anthelmintic efficacy testing by novel sampling strategies

- Faecal Egg Count Reduction Test for *Fasciola hepatica*

Tests for rapid DNA-based detection of specific pathogens and anthelmintic resistance

- *Haemonchus*
- *Fasciola*
- benzimidazole resistance
Key findings (2)

- Mathematical models were developed:
  - Helminth abundance and infection pressure models
    - *Ostertagia* in cattle, *Haemonchus* in sheep
  - GIS-based models to predict spatial and temporal distribution of GI nematodes and liver fluke
  - Conceptual models for worm control cost/benefit analysis
    - *Ostertagia* in dairy cows

- Field application of targeted selective treatment approaches and analysis of economic implications
Example of a useful model:

- **Nematodirus battus** in the UK

- Spring disease in lambs: high mortality and production loss.
- Timing of treatment is crucial.
- Hatching occurs in spring with rising temperature.

- **Predictions** based on soil and air temperature made available **in real time** to farmers and advisors on website (2013).
- Good uptake; to be refined and extended, and assessed for impact.
- Parallel approaches in other species.
What is PARAVAC?
- FP7 Project 2011-2015, 9 milj €
- Coordinator – Dave Knox (Moredun Institute)

Why PARAVAC?
- Develop **vaccines** to control helminth infections of livestock and reservoirs
  - *Haemonchus contortus*, *Ostertagia ostertagi*, *Cooperia oncophora* (GI nematodes)
  - *Dictyocaulus viviparus* (lungworm)
  - *Fasciola hepatica* (liver fluke)
  - *Echinococcus granulosus* (Hydatid worm, dog tapeworm)
- Provide a direct pipeline to **commercialisation** via Horizon 2020
<table>
<thead>
<tr>
<th>Parasite</th>
<th>Host</th>
<th>Source</th>
<th>Acronym</th>
<th>Nature</th>
<th>Efficacy as % reduction compared to controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemonchus contortus</td>
<td>sheep</td>
<td>gut</td>
<td>H11</td>
<td>aminopeptidase</td>
<td>&gt;90</td>
</tr>
<tr>
<td></td>
<td></td>
<td>gut</td>
<td>H-gal-GP</td>
<td>metallo, aspartyl &amp; cysteiny proteases</td>
<td>&gt;90</td>
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<tr>
<td>Ostertagia ostertagi</td>
<td>cattle</td>
<td>ES</td>
<td>ASP</td>
<td>nematode-specific protein</td>
<td>74</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>47</td>
</tr>
<tr>
<td>Cooperia oncophora</td>
<td>cattle</td>
<td>ES</td>
<td>ASP</td>
<td>nematode-specific protein</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>51</td>
</tr>
<tr>
<td>Fasciola hepatica</td>
<td>cattle</td>
<td>ES</td>
<td>CatL1</td>
<td>cysteiny protease</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>48</td>
</tr>
</tbody>
</table>
Why don’t we have commercial helminth vaccines?

- To date, all the vaccine proteins have been purified from worm extracts and ES
- No efficacious recombinant proteins (large scale production, cost reduction, stability)
- Lack of definition of protective immune responses (optimising vaccine delivery)
- Required efficacy not clearly defined
- Lack of business plan for commercialisation
Developing effective native or synthetic vaccines, the latter using novel molecular expression systems as required.

- Towards the first commercial vaccine against GI nematodes
  - *Haemonchus contortus* in sheep
  - Purified intestinal proteins
- Vaccine proteins produced in novel expression systems
  - Modified yeast *Pichia pastoris*
  - Free living nematode *Caenorhabditis elegans*
Defining the protective **immune responses** induced by these vaccines to optimise their structure and the method of **vaccine delivery**

- Identification of key **immune responses** for vaccine-induced protection
  - *Haemonchus contortus*: antibodies directed against worm intestines
  - *Ostertagia ostertagi* and *Cooperia oncophora*: Natural Killer cells
  - *Fasciola hepatica*: avidity of the antibody response

- Correct **3D structure** and folding required for effective synthetic vaccine production
Defining vaccine efficacy in housed and field trials

- **Vaccine efficacy tested in experimental infection trials**
  - Good protection: *F. hepatica, H. contortus, O. ostertagi, C. oncophora*

- **Field trials ongoing: proof of principle**
  - *Fasciola hepatica* recombinant vaccine in Ireland and Peru
  - *Cooperia oncophora* vaccine in Belgium

- **Computer models** to define required vaccine efficacy
  - *H. contortus* (sheep)
  - *F. hepatica* (cattle)
Implementation of novel solutions for helminth infections in ruminants

Needs

Solutions
FP6 & FP7

Implementation
Horizon 2020
Solution = integrated parasite control

Epidemiology
- Monitoring parasite infections
- Identify risk factors

Pharmacology, Parasitology
- New drugs
- Sustainable use of existing antiparasitics

Farm management
Integrated control of parasites in livestock
- Improved management of parasitic infections
- Vaccination
- Vaccines

Immunology & vaccinology
- Resistant cattle
- Identification of susceptible animals

Genetics

Economics
- Financial impact of infection & treatment

Horizon 2020

GLOWORM
PARASOL
PARAVAC
HORIZON 2020
PARASOL-GLOWORM-PARAVAC: Innovative worm control solutions for the EU livestock industry

PARASOL
Sustainable management of AR

PARAVAC
Novel solutions for immunoprotection

GLOWORM
Strategies for helminth control

Synthesis and systematic IMPLEMENTATION

Formulation of holistic worm control and farm management approaches

Industry wide communication and recommendation for best practice

Monitoring and feedback of implementation

Horizon 2020
Impact of worm infections on farm economics and animal welfare

Integrated parasite control

Estimate economic return of parasite control

Communication strategy

Increased farm profitability and animal welfare

Novel parasite control systems (Parasol, Gloworm, Paravac)

Farm management (genetics, nutrition, pasture management)
Risks

- Negative effect of helminth infections on livestock productivity and welfare, exacerbated by global changes (climate, management…)
- Failure to optimise anthelmintic usage and/or introduce alternatives could lead to loss of effective worm control.

Gaps

- Improved communication and implementation of holistic control strategies using improved diagnostics, host genetics, nutrition and pasture management to reduce the reliance upon anthelmintics.
- Introduction of novel sustainable control measures, e.g. vaccines, bio-active forages, nutraceuticals, ovidicals.