



The pathway to refining endpoints when assessing the efficacy of vaccines to a lethal disease of pigs (African Swine Fever)

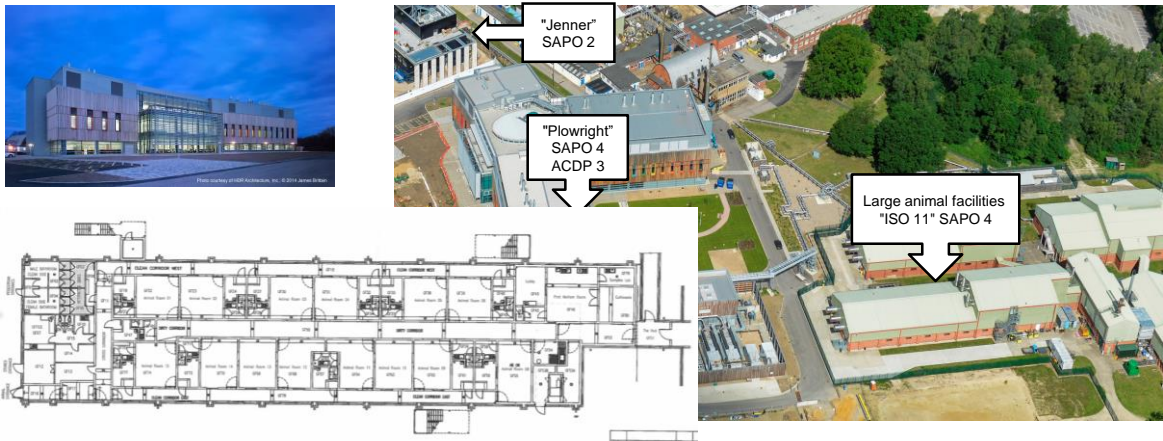
Ryan Waters – The Pirbright Institute



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The Pirbright Institute, UK

- “Preventing and controlling viral diseases”



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Summary

- What is ASF and why is it important?
- Controlling ASF
- Considerations around endpoints
- Current refinements to endpoints
- Take home messages

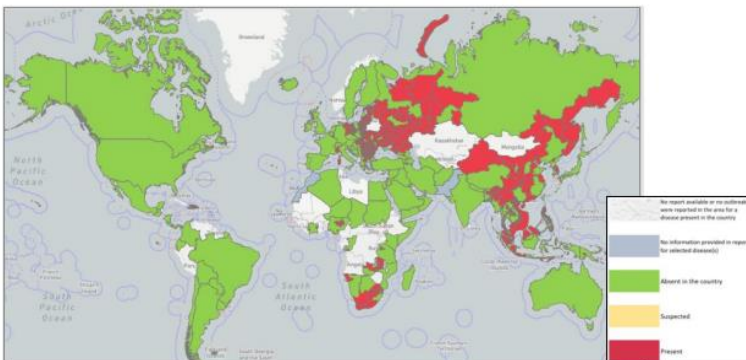


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What is ASF and why is it important?

- First identified in Kenya in 1921
- 1957, 1960, and 2007 incursion into Europe – since 2014 16 countries in EU have been affected
- 2018 detection in China, 2021 re-appearance in Americas after 40 years

ASF distribution in 2020-2022 (as of 1 April 2022) is shown in Figure 1.



OIE ASF situation report 9 – 7/4/2022



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What is ASF and why is it important?

- Highly contagious viral disease
- Complex virus >150 proteins
- Subclinical in warthogs – mortality approaching 100% domestic pigs 4-10dpi
- Direct and indirect transmission
- Devastation of both pig and human health and welfare
 - Affected animal welfare
 - Farms reliant upon homestead livestock for food and income
 - Estimated economic cost of UK outbreak £100 million
 - DEFRA / APHA Identified risk to UK pig population



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Controlling ASF

- Rapid diagnosis
- Increased biosecurity and stamping out
- Wild boar control
- **No commercially available vaccines**
- **No standardised approach to vaccine efficacy testing – Requirement to challenge pigs**

SECTION 3.9.

SUIDAE

CHAPTER 3.9.1.

**AFRICAN SWINE FEVER
(INFECTION WITH AFRICAN SWINE FEVER VIRUS)**

C. REQUIREMENTS FOR VACCINES

At present there is no commercially available vaccine for ASF.

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Considerations around endpoints

- **Scientific endpoint – protection from disease vs mortality**
 - Challenge virus
 - Vaccine candidate (e.g subunit vs LAV)
- **Humane endpoint – calibrate based on historic data of disease progression / publications – evidence based**

[J Am Assoc Lab Anim Sci](#). 2021 Jan; 60(1): 96–102.

PMCID: PMC7831341

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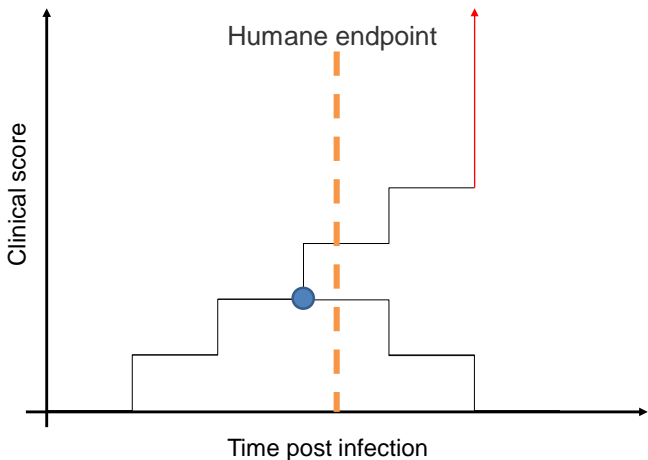
PMID: [33198851](#)

Clinical Indicators of Moribundity in Swine Experimentally Inoculated with African Swine Fever Virus

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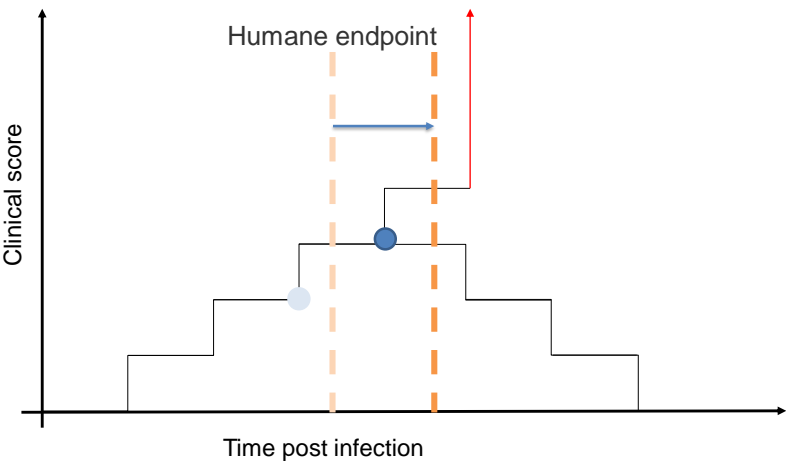
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Considerations around endpoints



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Considerations around endpoints



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Current refinements to endpoints

“Severe” end points

Date		
Indicators		
Temperature 4 th day		
- <39.0 (0)		
- 39.0 to 39.5 (1)		
- 39.6 to 40.0 (2)		
- 40.1 to 40.5 (3)		
- 40.6 to 41 (4)		
- >41 (6)		
Anorexia 2 nd day		
- Reduced eating (1)		
- Only picking at food (4)		
- Not eating (6)		
Behaviour 2 nd day		
- Lethargic (1)		
- Get up only when touched (2)		
- Slow to get up when touched (4)		
- Remain recumbent when touched (6)		
- Head hunched/arched		
Lameness 5 th day		
- Joint swelling (1) (if causing lameness= 1)		
- Severe swelling with difficulty walking (4)		
Respiratory 2 nd day		
- Laboured/increased breathing and/or coughing (1)		
- Severe (3)		
- Diarrhoea (1)		
- Bloody Diarrhoea (4) (Immediate endpoint)		
- Blood in Urine (4)		
- Vomiting (4)		
- Haemorrhagic areas on ears and body (1)		
- Generalised haemorrhage all over body (3)		
- Ocular discharge (1)		
Comments/Notes/Other		
Total	/40	/40

Clinical Sign	Description	Duration
Temperature	Pyrexia 40.5>	5 days
Anorexia	Non eating	3 days
Behaviour	Non response to stimuli	Instantly
Digestive system	Haemorrhagic diarrhoea Vomiting	Instantly 3 day of pyrexia (plus additional 2 signs)
Respiratory system	Respiratory failure	Instantly
Lameness	Non weight bearing Weight bearing	2 days after treatment if no improvements 5 days

“Moderate” end points

Clinical Sign	Description	Duration
Temperature	Pyrexia 40.5>	4 days (3 days when combined with one other sign)
Anorexia	Non eating	2 days
Behaviour	Slow / refuses to stand when touched	3 days
Digestive system	Haemorrhagic diarrhoea Vomiting	Instantly 3 days
Respiratory system	Increased breathing rate	2 days
Lameness	Non weight bearing Weight bearing	2 days after treatment if no improvements 5 days if no significant improvement
3 or more of the above signs		Instantly

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Future considerations

- Continue to collate data – peer review
- Standardise cell cultures for quantification of vaccines / challenge virus
- Formulate international agreement on ASFV vaccine assessment
- Use of biomarkers of disease progression – e.g. antigen quantification
- Telemetry / machine learning to assist behavioural analysis



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Take home messages

- Define scientific endpoints
- Define disease progression of model
 - Accurate data collection
 - Close communication with animal technicians
 - Clear humane endpoints – less subjective, more objective
 - Iterative process
- Communication
 - Include endpoints in publications
 - Attempts to standardise approaches

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