

**Supplementary Table 1: Primers used in this study for qPCR.**

Name	Sequence (5'-3')		
	Forward	Reverse	Probe or SYBR Green
<b>IBDV</b>	GAGGTGGCCGACCTCAACT	GCCCGGATTATGTCTTTGAAG	Probe: FAM- CCCCTGAAGATTGCAG GAGCATT-TAMRA
<b>IL-6</b>	AACATGCGTCAGCTCCTGAAT	TCTGCTAGGAATTCT CCATTGAA	SYBR Green
<b>IL-1<math>\beta</math></b>	GCTCTACATGTCGTGTGTGATGAG	TGTCGATGTCCCGCATGA	SYBR Green
<b>IL-8</b>	GCCCTCCTCCTGGTTTCAG	TGGCACCGCAGCTCATT	SYBR Green
<b>Mx1</b>	CACACCAACTGTCAGCGAT	ATGTCCGAAACTCTCTGCGG	SYBR Green
<b>IFN<math>\alpha</math></b>	CCACCGCTACACCCAGCACC	ATGGTGAGGTGAAGGTTGCGA	SYBR Green
<b>IFN<math>\beta</math></b>	CAGTCTCCAGGGATGCACAG	GAGAAGGTGGTGGTGAGAGC	SYBR Green
<b>RPLP0</b>	TTGGGCATCACCACAAAGATT	CCCACTTTGTCTCCGGTCTTAA	SYBR Green
<b>TBP</b>	CTTCGTGCCCCGAAATGCT	GCGCAGTAGTACGTGGTTCTCTT	SYBR Green

(E) indicates the bird should be euthanized immediately.

**Appearance:**

This is done by accumulative scoring.

Normal appearance	0
Pale comb / wattles	+1
Fluffed out feathers	+1
Eyes half shut	+1
Drooping wings / hunched / hangs head	+1
Laboured breathing	+1

**Behaviour without provocation:**

Select the score suited to the individual being assessed.

Normal posture	0
Crowds with group, but alert and social interactions with other birds evident, efforts made to seek water / feed in an independent manner.	1
Crowds within group, but lacking signs of normal social interaction / looking depressed, no efforts made to seek water / feed in an independent manner	2
Stands alone, depressed and no normal social interaction or independent action	3
Laid down alone, depressed and no normal social interaction or independent action	4
Collapsed with clear signs of severe distress	5 (E)

**Provoked behaviour:**

Select the score suited to the individual being assessed.

Normal (escapes capture by running)	0
Normal posture and attempts to avoid capture (escape attempted by walking)	1
Weak response to capture	2
No attempt to avoid capture but struggles when picked up	3
No attempt to avoid capture and lethargic when picked up	4
Fails to move when provoked	5 (E)

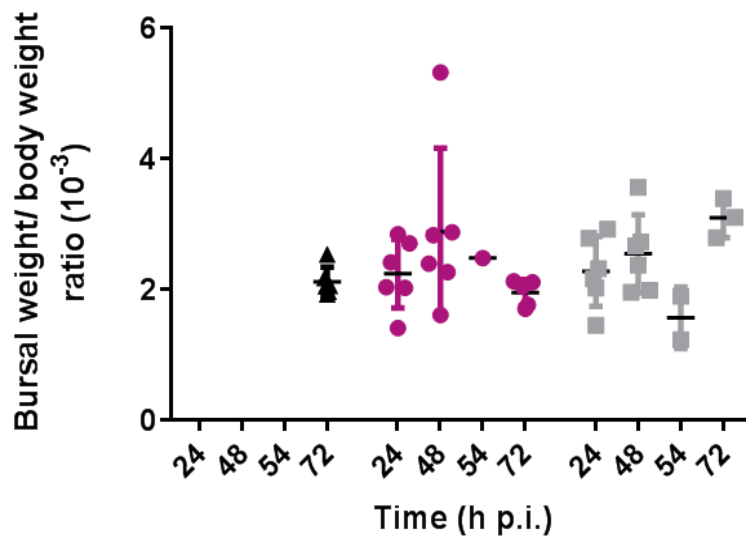
**Handling:**

This is done by accumulative scoring.

Feels normal	0
Fails to gain weight	+1
Evidence of weight loss	+1
Crop filled with water	+1
Soiled vent with classic white faecal material	+1

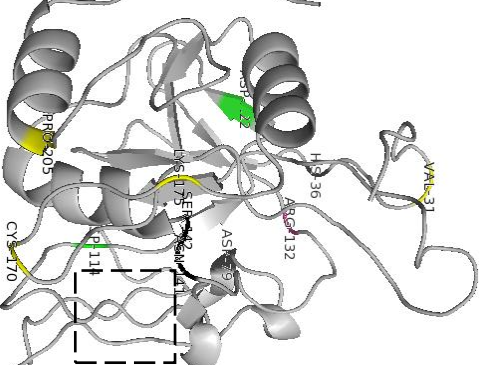
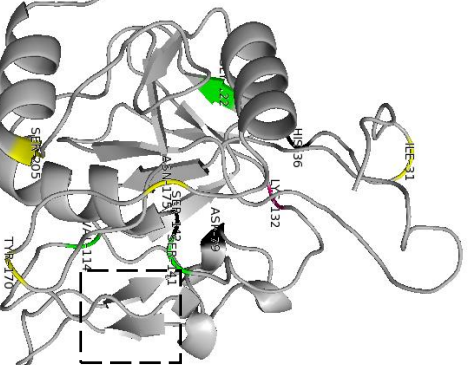
- Infected birds must be checked and weighed twice daily from the onset of clinical signs until after the infection has cleared and no more clinical signs are present. When no clinical signs are present, the birds can be checked once daily.
- Birds scoring 8-11 are classed as having moderate disease and must be checked every 8 hours
- Birds scoring 12-17 are classed as having have severe disease and must be checked every 3 hours
- Birds scoring 17 or E must be humanely culled.
- Birds scoring 12 for 3 days must be humanely culled.

**Supplementary Figure 1. Clinical Scoring system used in *in vivo* studies.** Birds were checked at least twice daily following inoculation by two independent observers and the clinical signs scored. Birds were humanely culled when their humane end-points were reached (a clinical score of 11 in this study).



**Supplementary Figure 2: No significant difference was observed between the Bursa of Fabricius: body weight (BF:BW) ratios of mock, F52/70- or UK661-inoculated birds.** Six birds per group were humanely culled at 24 and 48 hpi. One bird infected with F52/70 and three birds infected with UK661 were humanely culled at 54 hpi due to reaching their humane end points. The remaining infected birds were humanely culled at 72 hpi. 6 mock-infected birds were also humanely culled at 72 hpi. Birds were weighed and the bursa of Fabricius was removed at necropsy and weighed. The BF:BW ratio was determined and plotted for each bird. Horizontal lines represent the mean and error bars represent the standard error of the mean (SEM).

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**Supplementary Figure 3. There are nine amino acids different between the UK661 and the F52/70 VP4 proteins that cause differences to the predicted secondary structure of the molecule.** The amino acid sequences of five very virulent (grey), six classical (pink) and four cell-adapted (orange) IBDV strains were aligned by Clustal (GenomeNet) (A). Amino acids highlighted in yellow are exclusive to vvIBDV strains and those in pink are specific to F52/70 compared to all other strains. Residues highlighted in green are found in some but not all vvIBDV strains, and residues highlighted in blue indicate other amino acid differences in the VP4 sequences. The boxed regions are the catalytic triad responsible for the protease function of VP4. The Predicted UK661 (top) and F52/70 (bottom) VP4 structures based on the Yellowtail Ascites Virus VP4 (template 4izk.2.A) modelled using PyMol (B). Mutations between F52/70 and UK661 are labelled in the same colours as indicated in (A) and black sites indicate the location of the catalytic triad responsible for protease function. The dashed- boxed region shows examples of altered secondary structure, with alpha helices present in the UK661 VP4 molecule that are not seen in the F52/70 VP4 molecule.