Reference Policy Number: _____

Dear Sir/Madam,

The policy holder for the above policy wishes to enroll their horse/pony, currently insured with your company, in a research study.

The research study is a randomised placebo-controlled field vaccine trial of a *Clostridium botulinum* (*C. botulinum*) type C toxoid vaccine (BotVax C) for the prevention of Equine Grass Sickness (EGS) in a selected population of horses and ponies in Britain.

The field vaccine trial will be conducted under an Animal Test Certificate, granted by the Veterinary Medicines Directorate, and has been granted ethical approval by the Ethical Review Committees of the Animal Health Trust and the Universities of Edinburgh. Intended procedures within this study are in line with recognised veterinary practice as defined in The Animals (Scientific Procedures) Act 1986 and Royal College of Veterinary Surgeons Guide to Professional Conduct. Participation in the study will not affect routine veterinary preventive healthcare, or veterinary investigation and treatment of any disease or disorder occurring in enrolled horses/ponies during the study period. The Study Investigators and Study Monitor reserve the right to discontinue the trial at any time due to serious adverse events or welfare concerns.

This study will recruit a total of 1100 client-owned horses and ponies residing on premises previously affected by EGS. Using an equal parallel group design, the enrolled animals will be randomly selected to receive a primary course of three intramuscular injections at 21 day intervals, followed by a booster injection at 12 months, of either the test product BotVax C vaccine or a placebo. All horses and ponies will be checked by a qualified veterinary surgeon to ensure that they are in good health prior to entering the study and will be monitored closely for the entire duration of the study period. Enrolled horses and ponies will remain under the care of their owner/keeper, and under the care of the veterinary practice with which they are registered throughout the duration of the study period. Owners of horses/ponies enrolled in the trial will be instructed to seek veterinary attention for any health problems encountered during the trial, and will be provided with standardised study documentation for recording any clinical signs or behavioural changes observed in their horse/pony.

The *C. botulinum* type C toxoid vaccine (BotVax C) has been shown to be safe in horses as young as 3 months of age when given intramuscularly as directed. A study undertaken with 3-4 month old foals evaluated the safety of the vaccine. Ten foals were vaccinated 4 times at 3 week intervals with a 2ml intramuscular dose of vaccine. Five additional foals were injected with sterile saline control product, following the same administration schedule. Personnel evaluating the horses were blinded to vaccination status. All horses were monitored daily for general health and were evaluated on each day of vaccination, and for 2 days post-vaccination for fever, injection site reactions and clinical well-being. One horse vaccinated with the investigational product in this study displayed a slight swelling at the injection site after the second vaccination. This swelling could only be visualized when the horse held his head in a certain way. It was non-palpable, non-measurable, non-painful, and resolved within 4 days. This horse had been fractious in the stall while the immunisation was given and the needle had to be withdrawn during the immunisation for safety purposes. The remainder of the vaccination was given when the horse had calmed down, but this necessitated a second insertion of the needle. Importantly, no subsequent vaccinations resulted in further site reactions in this animal, suggesting that the resultant slight bump was a result of the improper administration of the vaccine. No other swellings or adverse events were noted during the study in any of the horses.

BotVax C vaccine and the adjuvanted placebo article to be used in the field vaccine trial have also been shown to be safe under conditions of field use. The Study Investigators have undertaken a 12 month duration pilot field vaccine trial, enrolling 95 privately owned horses and ponies (median age 6 years; range 6 months – 23 years) residing on 10 EGS-affected premises in North East Scotland. Enrolled horses/ponies were randomly assigned to test product vaccine (BotVax C) (n=48) or placebo (n=47) treatment groups. All 95 horses/ponies completed the primary treatment course of three 2ml intramuscular doses at 21 day intervals, and 87 horses/ponies received a booster treatment of a single 2ml intramuscular dose six months following the primary course, representing a total of 188 administered vaccine doses and 184 administered placebo doses. No systemic adverse reactions were reported, and no owner-reported local injection site abnormalities required treatment or received veterinary attention. The overall incidence of owner-reported abnormalities at the site of injection was 0.05 abnormalities per horse-week-at-risk, most frequently mild non-painful swelling at the injection site which resolved spontaneously within 1 – 2 days (reported in 3 horses/ponies in vaccine group and 3 horses/ponies in placebo group). There was no significant difference in the probability of an owner-reported abnormality between treatment groups (p=0.78).

All owners indicating an interest in participating in field vaccine trial have been advised that they are required to inform their insurance company prior to the start of the study. Owners have also been advised that they would be required to inform their insurance company of any disease, disorder or abnormalities (even those detected as incidental findings) detected during any of the veterinary health checks performed during the trial study period.

Should you require any further details regarding the field vaccine trial, prior to reviewing insurance cover for horses/ponies enrolled in the study, copies of the owner information documentation and study protocol are available on request to:

Dr Jo Ireland
Animal Health Trust
Lanwades Park
Kentford
Newmarket
CB8 7UU

Telephone: 01638 751000 (Extension 1239) Email: jo.ireland@aht.org.uk

Yours sincerely

Dr Jo Ireland BVMS PhD Cert AVP(EM) MRCVS
Equine Grass Sickness Research Co-ordinator, Animal Health Trust, Newmarket.

Dr Richard Newton BVSc MSc PhD FRCVS
Head of Epidemiology and Disease Surveillance, Animal Health Trust, Newmarket.

Professor Bruce McGorum BSc BVM&S PhD CEIM DipECEIM MRCVS
Head of Equine Section and RCVS Specialist in Equine Internal Medicine, Royal (Dick) School of Veterinary Studies & Roslin Institute, University of Edinburgh.

Professor Debbie Archer BVMS PhD CertES(soft tissue) DipECVS MRCVS
Professor of Equine Surgery, School of Veterinary Science, University of Liverpool.

Professor Chris Proudman MA VetMB PhD Cert EO FRCVS
Head of School and RCVS Specialist in Equine Gastroenterology, School of Veterinary Medicine, University of Surrey.