Nationwide field trial of a candidate vaccine for the prevention of Equine Grass Sickness

OWNER INFORMATION PACK

Equine Grass Sickness Surveillance

AHT Animal Health Trust

The University of Edinburgh

University of Liverpool

University of Surrey

Equine Grass Sickness Fund

Nationwide field trial of a candidate vaccine for the prevention of Equine Grass Sickness

Owner Information Pack

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Before you decide whether to participate in this research study, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and feel free to ask us if you would like more information or if there is anything that you do not understand. Please also feel free to discuss this with your friends, relatives and veterinary surgeon if you wish. We would like to stress that you do not have to accept this invitation and should only agree to take part if you want to.

Thank you for reading this.

For a full explanation of terms used in this information pack, please see the glossary of terms included at the end of the information pack (pages 19 – 22).

Section 1 – Introduction

Summary

- Equine grass sickness (EGS) is a frequently fatal disease affecting grazing horses, ponies and donkeys.
- The current theory is that EGS is a toxico-infectious form of botulism caused by the bacterium *Clostridium botulinum* type C, where a combination of risk factors triggers the production of toxins within the horse's intestinal tract.
- As EGS cannot be induced experimentally, a field vaccine trial is the only way to establish whether vaccination can be used to help prevent the disease.

- Only horses and ponies kept on premises with a previous history of EGS cases will be eligible to be enrolled in this nationwide field vaccine trial.
- This vaccine trial will follow 1100 horses and ponies for two years.
- Only horses and ponies in good general health will be enrolled in the vaccine trial.
- Pregnant mares or mares with foals at foot would not be enrolled in the vaccine trial.

- Half of the horses and ponies on the trial will be vaccinated with a *Clostridium botulinum* type C toxoid vaccine; the other half of the horses and ponies will receive an inactive placebo injection.
- Toxoid vaccines are made from inactivated toxic compounds, rather than the live bacteria. The candidate vaccine in this EGS field vaccine trial contains inactivated *Clostridium botulinum* type C toxins.
- The number of EGS cases occurring within the vaccinated group and within the placebo-treated group will be compared statistically to determine whether vaccination against *Clostridium botulinum* type C significantly reduces the risk of EGS.

- A minimum of six veterinary visits will be required for each enrolled horse or pony over the two year trial period.
- A minimum of eight short questionnaires about the management, preventive healthcare and health of each enrolled horse or pony would be required over the two year trial period.
- For a seven day period following each injection, we will ask owners to thoroughly check the injection site and record their findings.

- Previous safety and pilot studies have shown that both the *Clostridium botulinum* type C toxoid vaccine and the inactive placebo injection are safe. Only a small number of horses or ponies in these studies showed minor heat or swelling around the injection site for one or two days following injection.
- All veterinary fees directly related to the vaccine trial will be covered; however participating owners will remain responsible for the cost of any unrelated veterinary fees or other treatment.
- Unfortunately, it is possible that during the trial, a small number of enrolled horses/ponies may suffer fatal accidents or diseases. In fatal cases where EGS is suspected, the only way to confirm this diagnosis would be to perform a *post mortem* examination.

Introduction

Equine grass sickness (EGS) is a debilitating and often fatal disease affecting grazing horses, ponies and donkeys. EGS occurs predominantly, but not exclusively, in northern European countries and Great Britain has the highest incidence of EGS worldwide. Despite decades of research, we do not currently know definitively what causes EGS. Almost all cases of EGS occur in horses with access to grazing, and we think they are exposed to some form of noxious agent present in the soil and ingested as a contaminant of grass. There is growing scientific evidence to suggest that EGS may be caused by the bacterium *Clostridium botulinum* (*C. botulinum*) type C, which is found commonly within soil and is capable of producing a range of toxins, including potent neurotoxins (toxins that damage the nervous system), to which horses are particularly sensitive. The current theory is that EGS is a toxico-infectious form of botulism caused by *C. botulinum* type C, with the disease occurring when a combination of risk factors triggers the production of neurotoxin locally in the horse's intestinal tract.

Several research studies of EGS have demonstrated a protective effect of natural immunity to *C. botulinum* type C. In addition, other clostridial diseases, such as tetanus and botulism, are successfully prevented by vaccination, suggesting that it should theoretically be possible to prevent EGS by vaccination. It is not possible to assess the efficacy of a candidate vaccine for the prevention of EGS experimentally, as it is not possible to artificially reproduce the disease. Therefore, a field vaccine trial represents the only available method of evaluating the preventive effect of vaccination and testing the theory that *C. botulinum* type C toxico-infection causes EGS.

In this nationwide EGS vaccine trial, horses and ponies would be randomly selected to join one of two equally sized groups: either the vaccine group (vaccinated with the *C. botulinum* type C toxoid vaccine) or the placebo-treated group (receiving an inactive placebo injection). The number of EGS cases occurring within the vaccinated group and within the placebo-treated group will be compared statistically to determine whether vaccination against *C. botulinum* type C significantly reduces the risk of EGS. It is exceptionally rare for any vaccination to offer complete protection against a disease, and some horses and ponies' immune systems respond less well to vaccination than others, meaning that they may be less well protected. Therefore it would be expected that cases of EGS could occur throughout the vaccine trial in both the vaccinated group and the placebo-treated group; however if the vaccine is effective in preventing EGS, the number of EGS cases in the vaccinated horses and ponies would be significantly lower.

What is the purpose of the study?

Commencing in 2014, we will undertake a large scale, nationwide vaccination trial of a candidate *C. botulinum* type C toxoid vaccine, involving at least 1100 horses and ponies over a two year period.

The main purpose of this EGS field vaccine trial is to evaluate the efficacy of *C. botulinum* type C vaccination in preventing naturally occurring EGS in Great Britain.

The specific objectives of this study are:

1) To compare the frequency of EGS cases occurring in horses and ponies vaccinated with the candidate *C. botulinum* type C toxoid vaccine with the frequency of EGS cases in horses and ponies residing on the same premises which receive an inactive placebo injection. This comparison will allow us to determine whether vaccination against *C. botulinum* type C significantly reduces the incidence of EGS.
2) To use pre- and post-vaccination antibody levels in blood samples to measure the immune response to vaccination with the candidate *C. botulinum* type C toxoid vaccine.

Why have I been invited to take part?

We are aiming to enrol a total of 1100 horses and ponies for this EGS field vaccine trial. Horse and pony owners keeping their animals on premises with a history of a high number and frequency of EGS cases are being invited to participate in this new research study. Premises affected by EGS have been identified in several ways:

1) via information provided to the EGS Surveillance Scheme by owners and registered veterinary practices
2) via equine veterinary surgeons attending cases of EGS
3) via specialist equine veterinary surgeons from the University of Edinburgh or the University of Liverpool treating EGS cases
4) via information held by the EGS Fund

Should you wish to participate in this EGS field vaccine trial, we will contact your veterinary practice directly and invite them to take part.

If you are interested in taking part in the EGS field vaccine trial, there are several criteria for including horses or ponies in the trial that you need to consider:

If there have been no cases of EGS on the premises where you keep your horse/pony within the last 3 years, you would not be eligible for participation in this trial.

Horses and ponies, of any gender and of any breed, will be enrolled in the EGS vaccine trial if:

- they have a valid passport that complies with the Horse Passports Regulations 2009. Part II of Section IX of the passport must state the animal is not intended for human consumption and must be signed by the owner and officially countersigned by an authorised individual

  For more information, or to check if your horse/pony's passport is valid, please consult the Department for Environment Food & Rural Affairs website http://archive.defra.gov.uk/foodfarm/farmanimal/movements/horses/horses_qa.htm or the Gov.UK website https://www.gov.uk/horse-passport

- they are in good general health

Donkeys, asses, mules or zebras WILL NOT be included in the trial.

Horses and ponies will not be enrolled in the EGS vaccine trial if:

- their identification cannot be verified by microchip number or passport identification sketch
- they do not have a valid passport
- they are intended for human consumption as stated in Section IX of the passport
- Part II of Section IX of their passport has not been signed by the owner and officially countersigned by an authorised individual
- they are foals less than six months of age
- they are pregnant or lactating mares
- they have suffered from EGS in the past
- their owner would not be willing to consent to a full *post mortem* examination if at any point during the trial they died or had to be put to sleep due to EGS

Do I have to take part?

We hope you will be able to participate in this EGS field vaccine trial, which is entirely voluntary and you are free to withdraw from the study at any time, without explanation.

If my horse or pony is insured, will taking part in the trial affect my insurance policy?

If your horse/pony is insured, **you will be required to inform your insurance company prior to the start of the EGS field vaccine trial.** We have consulted several insurance companies, via the Equine Insurance Forum and we will be able to provide you with a document detailing the trial for your insurance company. The insurance company may then:

a) Make a note of the information and keep the policy running in accordance with its normal terms and conditions.
b) Extend the policy to cover any additional risk due to participation in the trial and charge an additional premium.
c) Place a policy exception to exclude from cover any cause of additional risk as a result of participating in the trial. You could then request removal of the exclusion at the end of the trial period.
d) Cancel the policy returning the premium for the unexpired period.

Most insurance companies attending the Equine Insurance Forum indicated that they would proceed with options a, b, or c and it is unlikely that your insurance company would elect to cancel your policy. As the premises where you keep your horse or pony have previously experienced a case of EGS, it is possible that some sort of exclusion related to EGS is already in place on your insurance policy.

You would also be required to inform your 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.

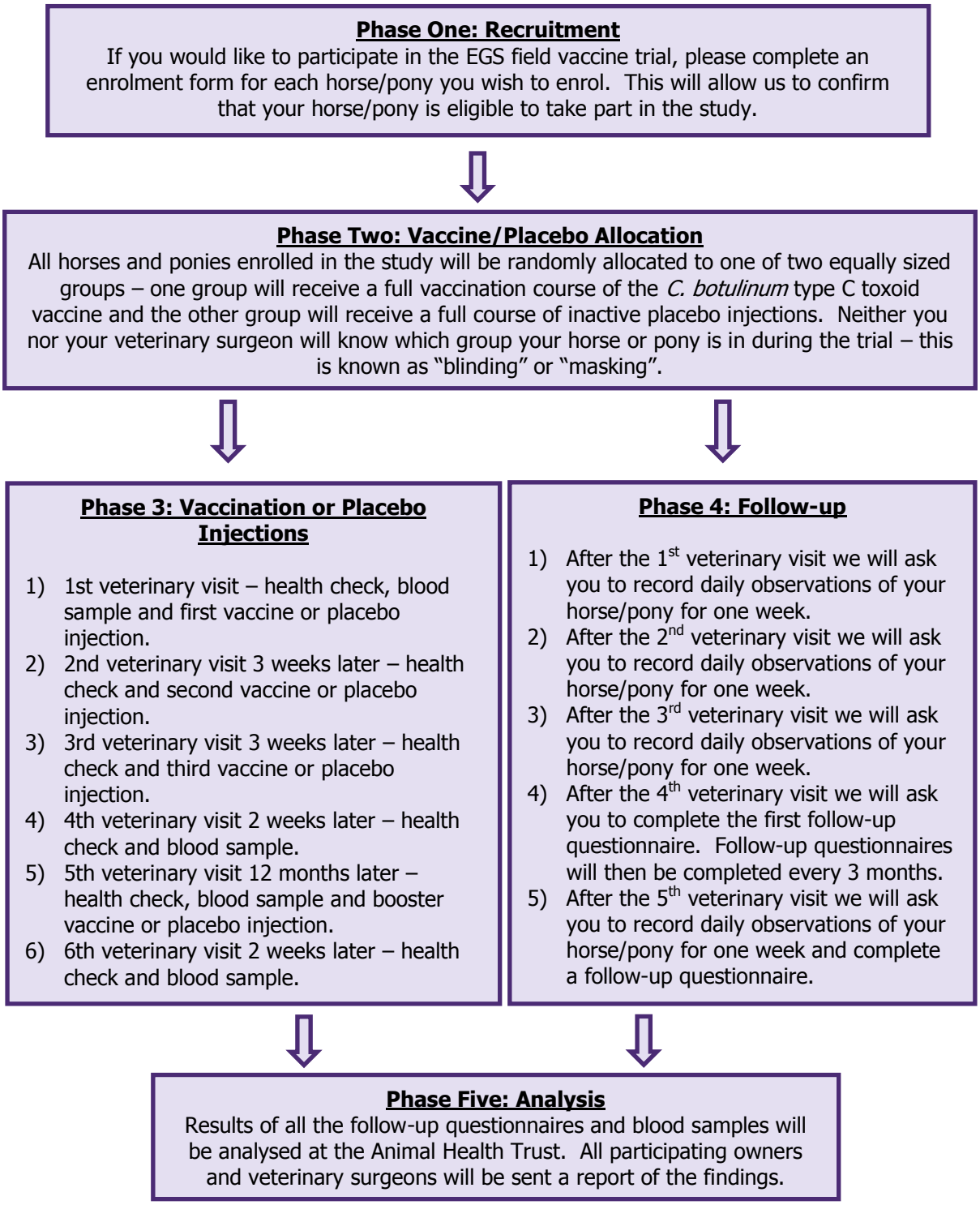
Section 2 – About the EGS Field Vaccine Trial

What will happen if I take part?

This EGS field vaccine trial will be conducted by the Animal Health Trust in collaboration with the Universities of Edinburgh, Liverpool and Surrey. The EGS field vaccine trial has been authorised under an Animal Test Certificate issued by the Veterinary Medicines Directorate and has received ethical approval from the Animal Health Trust Clinical Research Ethics Committee and the University Of Edinburgh School Of Veterinary Medicine Ethical Review Committee.

If you decide to take part in the EGS field vaccine trial, there will be several phases involved over a minimum study period of two years (illustrated in Figure 1). These phases of the EGS field vaccine trial are described in greater detail below. We would ask you to maintain a record or diary with information regarding your horse/pony's normal behaviour, appetite, water intake, droppings and urination. This will make it easier for you to detect any changes in your horse/pony's normal health and behaviour during the study. We would also ask you to record any changes you make to your horse/pony's management throughout the study, such as feeding, exercise regime, field turnout or stabling and any healthcare you provide such as worming or vaccinations. Approximately once every three months, we will contact you to complete a short telephone questionnaire about your horse or pony's management and health.

Figure 1: Phases involved in the EGS field vaccine trial for a candidate *C. botulinum* type C toxoid vaccine against EGS.



Phase One: Recruitment

Once you have read the owner information pack, if you wish to participate in the EGS field vaccine trial, we would ask you to complete and return a short questionnaire (enrolment form) about your horse or pony, and the premises on which they are kept. This will allow us to ensure that all horses and ponies you wish to enrol on the study are eligible to take part. After we receive your completed enrolment form(s), we will contact you to conduct a short telephone questionnaire to gather further important information regarding the health and management of your horse/pony.

Please ensure your horse/pony has a <u>valid passport</u> before enrolling them in the EGS field vaccine trial.

All horses and ponies enrolled in the trial will remain under the care of their normal veterinary practice and this study will not interfere with routine preventive healthcare or treatment of any conditions throughout the entire duration of the trial. Therefore, if you wish to take part in the trial, we would contact your veterinary practice directly to invite them to participate. Your veterinary practice would then receive a complete trial information pack.

Phase Two: Vaccine/Placebo Allocation

Once eligible horses and ponies are enrolled on the trial, they will be assigned a unique identification number. Using computer-generated random numbers, your horse or pony would be randomly selected to join one of two equally sized groups: either the vaccine group (vaccinated with the *C. botulinum* type C toxoid vaccine) or the placebo-treated group (receiving an inactive placebo injection). This process is referred to as "randomisation" and it ensures that the only difference between the two groups is whether they receive the vaccine or the placebo. Several risk factors for EGS have been identified in previous research studies and without proper randomisation it could be possible that existing risk factors for EGS might affect our ability to determine how effective the vaccine is.

The *C. botulinum* type C toxoid vaccine is very similar to the tetanus toxoid vaccine commonly used to prevent tetanus in horses and ponies. The placebo injection will have a similar appearance to the *C. botulinum* type C toxoid vaccine but will not contain the active component (or "antigen"). This placebo will be harmless, but will not provide any immunity or protection against EGS. Having a group of placebo-treated horses and ponies is vital in a trial to evaluate the effectiveness of a vaccination against EGS. The results obtained in the two groups are compared at the end of the study to see if the vaccine treatment is more effective in preventing EGS than the placebo injection.

In order to ensure the scientific validity of the vaccine trial, neither you nor your veterinary surgeon will be informed of the group to which your horse or pony has been selected to join. This procedure is commonly referred to as "blinding" or "masking" and is very important to ensure that the findings of the vaccine trial are not influenced in any way by the expectations of people taking part. For example, a veterinary surgeon might be more likely to suspect EGS in a horse suffering from colic if he/she knew that that particular horse had received the inactive placebo injection. Conversely, a veterinary surgeon may think EGS was a less likely diagnosis in a horse with colic that had received the *C. botulinum* type C toxoid vaccine, as he/she might expect that the vaccine would have reduced the risk of EGS in vaccinated horses and ponies. Without including a placebo group, it would be very difficult to ensure that owners and veterinary surgeons did not know what treatment each horse or pony received.

Phase Three: Vaccine/Placebo Administration

Over the two year period, several veterinary visits will be required at specific time points and all enrolled horses and ponies will receive a total of four injections. At some of the scheduled veterinary visits, described below, your veterinary surgeon would also take a blood sample from your horse or pony. We hope that your usual veterinary practice will be able to carry out each visit, but if this is not feasible for any reason, it may be possible for specifically trained vaccine trial veterinary surgeons to attend your horse or pony. For each visit you, or someone you have nominated to act on your behalf, would be required to be present to hold your horse or pony. Each visit would be booked in advance with your veterinary practice, at a date and time within their usual working hours.

All horses and ponies included in the trial must be in good general health at initial veterinary clinical examination, and those in poor condition or exhibiting signs of disease will be excluded at this stage. As corticosteroids can affect the immune system, horses or ponies would not be given the vaccine or placebo injection within two weeks of administration of any form of corticosteroid treatment.

Why would my horse or pony have a blood sample taken?

We know from previous research studies that there is an association between the risk of EGS and both worm burden and the use of certain types of wormers; however the exact nature of this relationship is not clear. In order to establish the worm burden of all enrolled horses and ponies, blood samples will be collected at certain times throughout the vaccine trial to check for tapeworm antibody levels at Diagnosteq, University of Liverpool. We will then send the results of this tapeworm blood test to you and to your veterinary surgeon, allowing them to give you advice about targeted worm control and the most appropriate wormers to use for your horse or pony.

Before the first vaccine or placebo injection and following the final booster vaccine or placebo injection, your veterinary surgeon will perform an additional health check and take a blood sample for a routine health screen. Following measurement of tapeworm antibody levels, and the pre and post-trial health screens, any surplus blood sample remaining will be stored at the Animal Health Trust. In collaboration with the Universities of Edinburgh and Liverpool, the Animal Health Trust have developed tests for measuring antibody levels to *C. botulinum* type C antigens, which will be used with any surplus blood samples to measure immune responses to the *C. botulinum* type C toxoid vaccine in vaccinated horses and ponies.

What will be included in the veterinary health checks?

You will need to ensure that your horse/pony's valid passport is available for each veterinary visit throughout the EGS field vaccine trial. At each visit, your veterinary surgeon will perform a health check for your horse or pony (for more details please see Table 1 below). This examination should take approximately 10 minutes and will include: using a weigh tape to estimate your horse/pony's weight; assessment of body condition score; assessment of general demeanour; taking their temperature; listening to heart and lungs and noting heart and respiratory rate; checking lymph nodes ("glands"); examination for any discharge from the nose or eyes; and asking you questions regarding your horse/pony's recent health, appetite, thirst, urination and faeces.

Phase Four: Follow-up and Monitoring

Throughout the EGS field vaccine trial we would like you to let us know about any changes in the management and health of your horse and pony. For a one week period following each injection your horse/pony receives, we would ask you to perform a daily inspection, assessing their appetite, general wellbeing and the site of the injection. We would then ask you to complete a post-treatment observation recording form (example shown in Figure 2) and return the form to the Animal Health Trust. Your veterinary surgeon will be able to show you how to perform these checks and guidelines for how to perform post-treatment observations and record your findings can be found in the appendix on pages 23 – 24.

Throughout the EGS field vaccine trial we would also like you to record details of all routine healthcare that your horse/pony receives, such as routine vaccinations and wormers. We will provide you with healthcare forms to complete and return to the Animal Health Trust. We will also contact you at regular intervals (approximately once every three months) to complete short telephone questionnaires about your horse/pony's management and health.

Figure 2: Example of the post-treatment observation recording form that we would ask you to complete for your horse/pony following each vaccine/placebo injection.

Equine Grass Sickness Vaccine Trial

Post-treatment Observation Recording Form

Owner name: SMITH

Horse name: MISTY

Horse ID: 0000001 Premises ID: 0001

Area		Observation	Score
Feeding		0 = normal, 1 = reduced appetite, 2 = off feed	0, 1, or 2
Demeanour		0 = normal, 1 = depressed, 2 = markedly depressed	0, 1 or 2
Injection site reaction	**Heat**	0 = none, 1 = slight, 2 = moderate, 3 = severe	0, 1, 2 or 3
	Pain	0 = none, 1 = slight, 2 = moderate, 3 = severe	0, 1, 2 or 3
	Swelling	0 = none, 1 = slight, 2 = moderate, 3 = severe	0, 1, 2 or 3
Other		0 = none, 1 = other observation/clinical sign present	0 or 1

On the day of vaccination, please make first daily observations 1 to 3 hours following injection and on subsequent days at approximately 24 hour intervals thereafter

Week 1/Week commencing_____

Observation	**Day 0:** 1st Injection	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**
Feeding Score	0	0	0	0	0	0	0
Demeanour Score	0	0	0	0	0	0	0
Injection Site: Heat	0	0	0	0	0	0	0
Injection Site: Pain	0	0	0	0	0	0	0
Injection Site: Swelling	0	1	1	0	0	0	0
Other (please specify below)	0	0	0	0	0	0	1
Other observations	Coughed twice on day 6 after 1st injection – has dust allergy and had dry hay day before						

Table 1: Schedule for veterinary visits for each vaccine/placebo injection.

	What happens at the veterinary visit?	**What will happen after the veterinary visit?**
1st veterinary visit	Your veterinary surgeon will visit and: ▪ check your horse/pony's passport to confirm their identity and to ensure that the declaration that they are not intended for human consumption has been completed correctly ▪ perform a health check on your horse/pony (as described on page 8) and complete a pre-treatment clinical examination form ▪ take a blood sample from your horse/pony for a pre-trial health screen ▪ administer the first vaccine or placebo injection to your horse/pony by intramuscular injection in the neck	After the 1st veterinary visit we will ask you to: ▪ record daily observations of your horse/pony for one week (as described in the appendix on pages 23 – 24)

2nd veterinary visit **3 weeks later**	Your veterinary surgeon will visit and: ▪ check your horse/pony's passport to confirm their identity ▪ perform a health check on your horse/pony and complete a pre-treatment clinical examination form ▪ administer the second vaccine or placebo injection to your horse/pony by intramuscular injection in the neck	After the 2nd veterinary visit we will ask you to: ▪ record daily observations of your horse/pony for one week
3rd veterinary visit **3 weeks later**	Your veterinary surgeon will visit and: ▪ check your horse/pony's passport to confirm their identity ▪ perform a health check on your horse/pony and complete a pre-treatment clinical examination form ▪ administer the third vaccine or placebo injection to your horse/pony by intramuscular injection in the neck This will be the final injection of the primary course of vaccination or placebo treatment.	After the 3rd veterinary visit we will ask you to: ▪ record daily observations of your horse/pony for one week Your veterinary surgeon will discuss with you your horse/pony's health screen blood test results.
4th veterinary visit **2 weeks later**	Your veterinary surgeon will visit and: ▪ check your horse/pony's passport to confirm their identity ▪ perform a health check on your horse/pony ▪ take a blood sample from your horse/pony to check for tapeworm antibody levels	After the 4th veterinary visit we will ask you to: ▪ complete a follow-up telephone questionnaire You will also receive your horse/pony's tapeworm blood test results.
5th veterinary visit **12 months later**	Your veterinary surgeon will visit and: ▪ check your horse/pony's passport to confirm their identity ▪ perform a health check on your horse/pony and complete a pre-treatment clinical examination form ▪ take a blood sample from your horse/pony to check for tapeworm antibody levels ▪ administer a booster vaccine or placebo injection to your horse/pony by intramuscular injection in the neck	After the 5th veterinary visit we will ask you to: ▪ record daily observations of your horse/pony for one week ▪ complete a follow-up telephone questionnaire You will also receive your horse/pony's tapeworm blood test results.
6th veterinary visit **2 weeks later**	Your veterinary surgeon will visit and: ▪ check your horse/pony's passport to confirm their identity ▪ perform a health check on your horse/pony ▪ take a blood sample from your horse/pony for a post-trial health screen	Your veterinary surgeon will discuss with you your horse/pony's health screen blood test results.

Phase Five: Analysis

Results of all the follow-up questionnaires and blood samples will be analysed at the Animal Health Trust. The EGS incidence rate (number of EGS cases over the vaccine trial study period) will be compared for the group of horses and ponies receiving the candidate *C. botulinum* type C toxoid vaccine and those receiving the inactive placebo injection. These results will demonstrate whether or not the candidate *C. botulinum* type C toxoid vaccine is effective in preventing EGS. The researcher undertaking these statistical analyses will not be aware of which group of horses and ponies received the *C. botulinum* type C toxoid vaccine and which received the inactive placebo, in the same way that participating owners and veterinary surgeons are "blinded" or "masked" to the treatment group allocations. This again ensures that the findings of the vaccine trial are not influenced in any way by the expectations of people taking part.

Following final analysis of the results of this vaccine trial, we will inform you of which treatment group your horse/pony was allocated to, and all participating owners and veterinary surgeons will be sent a report of the findings of the EGS field vaccine trial.

Section 3 – About Your Participation in the EGS Field Vaccine Trial

Will there be any cost involved in taking part in the EGS field vaccine trial?

Should you decide to participate in the EGS field vaccine trial, no personal expenses or reimbursements will be provided to you.

You will remain responsible for the cost of:

- All routine healthcare for your horse or pony, such as influenza or tetanus vaccinations, wormers, dental care, feeding etc. throughout the EGS field vaccine trial.
- Any veterinary or other treatment costs for any disease or injury not directly related to the vaccine trial at any point during the EGS field vaccine trial. Details of examinations and treatments undertaken, provided to us by your veterinary surgeon, will allow us to determine whether or not the disease or injury is directly related to the vaccine trial.
- Any veterinary or other treatment costs for unrelated conditions for which you request attention during a scheduled vaccine trial veterinary visit (for example, if you request that your veterinary surgeon examines your horse/pony due to a health problem such as lameness during a scheduled vaccine trial visit, you would be responsible for the cost of this additional examination and any resulting treatment or further diagnostic tests).
- The cost of insuring your horse/pony, if applicable.

However, there will be no cost to participating horse and pony owners for:

- Veterinary visits made for the administration of trial vaccinations/placebo injections.
- Vaccine trial *C. botulinum* type C vaccinations or inactive placebo injections.
- Veterinary health checks before each trial vaccination or inactive placebo injection.
- Tapeworm blood tests and routine health screen blood tests.
- Additional veterinary visits and veterinary investigation and treatment of any suspected reactions to the trial *C. botulinum* type C vaccination or inactive placebo injection.
- Additional veterinary visits, veterinary investigation and treatment of any suspected case of EGS. However, the cost of colic surgery or exploratory abdominal surgery WOULD NOT be covered by the trial.
- Veterinary investigation, transport costs and *post mortem* examination should your horse or pony die, or have to be put to sleep, during the trial period due to suspected EGS. The cost of individual cremation WOULD NOT be covered by the trial.

If you wish to make a contribution towards the cost of the EGS vaccine trial, please consider making a donation to the Equine Grass Sickness Fund, where further information can be found on their website at: http://www.grasssickness.org.uk/donate/

Are there any risks in taking part?

At any point during the EGS field vaccine trial, if there are any concerns regarding the safety of the *C. botulinum* type C toxoid vaccine or the inactive placebo injection, the trial will be stopped immediately.

A safety study of the *C. botulinum* type C toxoid vaccine has already been undertaken. No significant reactions to the vaccine were observed during the course of this study, and only one horse had a very mild local reaction at the injection site. A pilot field vaccine trial involving 95 horses and ponies has also been undertaken, in which the frequency of mild local injection site reactions was low. Local reactions at the site of injection, such as slight swelling, heat or pain, can sometimes occur following intramuscular injections in horses and ponies.

For both the *C. botulinum* type C toxoid vaccine and the inactive placebo injection in this vaccine trial, as with the administration of any type of intramuscular injection, there is a risk of:

- injury to people handling the horse/pony and the veterinary surgeon at the time of injection.
- a local adverse reaction at the site of injection. These reactions may involve localised heat and/or pain and/or swelling at the injection site, or stiffness of the neck. Only one mild local injection site reaction was observed during a previous safety study using the *C. botulinum* type C toxoid vaccine. In the pilot field vaccine trial, no local injection site reactions required any form of treatment or veterinary attention. These mild local injection site reactions all resolved spontaneously without treatment in 1 to 2 days and included slight heat at the injection site, slight swelling or mild discomfort at the injection site within the first 1 to 3 days following injection.
- an adverse systemic reaction, where the entire body may be affected and the horse or pony may become unwell. No adverse systemic reactions were observed during a previous safety study using the *C. botulinum* type C toxoid vaccine. No adverse systemic reactions were observed during the pilot field vaccine trial using the *C. botulinum* type C toxoid vaccine.

If your horse/pony has experienced any reaction following any vaccination or other injection at any time in the past, or if your horse/pony is "needle shy" or difficult to inject, please discuss this with your veterinary surgeon and/or the study staff prior to deciding whether or not to participate in the trial.

If you have any concerns about the risks involved in this EGS field vaccine trial, please discuss these with your veterinary surgeon and/or the study staff prior to deciding whether or not to participate in the trial.

Is there any risk of EGS for horses and ponies taking part?

Participating premises will be selected based on a high number and frequency of EGS cases, therefore all enrolled horses and ponies will be at increased risk of EGS compared to horses and ponies kept on premises with no history of EGS. However, there is **no increased risk of EGS** as a result of administration of either the candidate *C. botulinum* type C vaccine or the inactive placebo injection.

What happens if my horse or pony has any health problems during the trial?

If you have **any concerns regarding the health of your horse/pony** during the EGS field vaccine trial, **you should contact your veterinary practice immediately.**

If you suspect your horse/pony has had any form of reaction to the vaccination or placebo injection, you should contact your veterinary practice immediately. Your veterinary surgeon will then arrange to visit your horse/pony and perform a clinical examination and administer any treatment required. Your veterinary surgeon will then provide a report of the clinical examination and treatment administered to the study staff.

At any point during the EGS field vaccine trial, if you are concerned that your horse/pony may be displaying clinical signs of EGS, you should contact your veterinary practice immediately. Your veterinary surgeon will then arrange to visit your horse/pony and perform a clinical examination, any necessary further tests and administer any treatment required. Your veterinary surgeon will then provide a report of the clinical examination, any diagnostic tests performed and treatment administered to the study staff. Where a diagnosis of chronic EGS is suspected, an additional veterinary examination by a specialist equine veterinary surgeon from the Animal Health Trust, the University of Edinburgh or the University of Liverpool would be required to obtain clinical confirmation of this diagnosis.

Unfortunately, it is possible that during the trial, a small number of enrolled horses/ponies may suffer fatal accidents or diseases. In cases where EGS is suspected, you may be aware that the only way to confirm this diagnosis would be to perform a *post mortem* examination. Should this happen, we would organise collection and transportation to the Animal Health Trust, the University of Edinburgh or the University of Liverpool for *post mortem* examination. Following a *post mortem* examination, it is often not possible to organise individual cremation, and where individual cremation is possible, this additional cost would not be covered by the trial, due to constraints on trial funding.

Should your horse/pony die, or have to be put to sleep during the EGS field vaccine trial, compensation or reimbursement for the cost of your horse/pony **would not be provided**.

What if I am unhappy or if there is a problem?

During the vaccine trial, should you experience any difficulties with regard to your on-going participation, or concerns about your horse or pony's enrolment in the trial, you should make this known to either your veterinary surgeon or the study staff immediately.

If you are unhappy or have any problem regarding your participation in the EGS trial, please contact:
Dr Jo Ireland
Centre for Preventive Medicine
Animal Health Trust
Lanwades Park
Kentford
Newmarket, CB8 7UU
Email: jo.ireland@aht.org.uk
Telephone: 01638 751000 (Ext 1239)

If you remain unhappy or have a complaint which you feel you cannot come to us with then you should contact the Animal Health Trust, where a member of staff not involved with this study will be able to deal with your complaint. When contacting the Animal Health Trust, please provide details of the name or description of the study (so that it can be identified), the researcher(s) involved, and the details of the complaint you wish to make. Telephone: 01638 751000

If you have any concerns about the health of your horse or pony, please <u>contact your veterinary surgeon immediately</u>.

Your veterinary surgeon will contact the trial study staff and we will then contact you directly to discuss whether or not it is possible for your horse or pony to continue the trial.

Will my participation be kept confidential?

Your participation will be completely confidential. Your veterinary surgeon will discuss any findings from their examination of your horse/pony with you directly, before sharing these with the study staff. All information that you provide will be maintained and analysed at the Animal Health Trust and will only be used for the purposes of this study. The information that your veterinary surgeon provides regarding your horse/pony will be completely confidential, will be maintained and analysed at the Animal Health Trust and will only be used for the purposes of this study. Information will only be shared between the University of Edinburgh, University of Liverpool, University of Surrey and the Animal Health Trust and only dedicated study staff at these institutions will have access to this information. All information collected during the EGS field vaccine trial will be anonymised and data will be stored on a password protected desktop computer on the secure Animal Health Trust network. Horse and pony data, which is not covered by the Data Protection Act, will be stored using individual unique identification numbers only. Completed telephone questionnaires will be stored in a locked filing cabinet in a locked archive office within the Epidemiology and Disease Surveillance department at the Animal Health Trust. Only EGS field vaccine trial researchers will have access to the data, which will be stored at the Animal Health Trust for a maximum of ten years and thereafter disposed of by a high security confidential waste shredding and recycling commercial company.

What will happen to the results of the study?

We will let you know the results of the vaccine trial in a newsletter that will be sent out after the study is completed. It is hoped that findings from this EGS field vaccine trial will be published in an appropriate peer reviewed veterinary scientific journal. No individual premises, owners, veterinary surgeons or horses/ponies will be identifiable in any published reports of this trial. The results may also be used within an application to the Veterinary Medicines Directorate for a Marketing Authorisation for the candidate *C. botulinum* type C toxoid vaccine, allowing it to be placed on the market for sale.

What will happen if I want to stop taking part?

Should you decide to participate in the EGS field vaccine trial, you are free to withdraw yourself or your horse/pony at any time, without explanation. Results up to the period of withdrawal may be used, if you are happy for this to be done. Otherwise you may request that they are destroyed and no further use is made of them.

What will happen if my horse/pony is sold or put on loan during the study?

If your horse/pony is sold, put out on loan, or a horse/pony you have on loan returns to their owner during the study, please inform the study staff immediately. Results up to the point where you are no longer the owner/keeper may be used, if you are happy for this to be done and we will issue you with an information pack about the trial to send to the new/owner keeper.

What will happen if I move my horse/pony to different premises during the study?

If you move your horse/pony to different premises, please inform the study staff immediately. We will contact you to complete another short telephone questionnaire about the new premises. If the new premises to which you have moved your horse/pony meet the inclusion criteria for the study, it may be possible for your horse/pony to remain enrolled in the EGS field vaccine trial, and we would require details of any change to the veterinary practice with which your horse/pony is registered. If the new premises do not meet the inclusion criteria for the study, your horse/pony would no longer be enrolled in the vaccine trial; however we would like you to continue to inform us of any changes in your horse/pony's health. Results up to the point when they moved to new premises may be used, if you are happy for this to be done.

Section 4 – Frequently Asked Questions (FAQs)

What type of vaccine is being used in the nationwide EGS vaccine trial?

The vaccine used in this EGS field vaccine trial is a toxoid vaccine, containing inactivated *Clostridium botulinum* type C toxins. This vaccine is very similar to the tetanus toxoid vaccine commonly used to prevent tetanus in horses and ponies.

Can the vaccine cause EGS?

No – because the vaccine contains **inactivated** *Clostridium botulinum* type C toxins, it would not be possible for the vaccine to cause EGS.

How can you tell if the vaccine prevents EGS?

EGS cannot be reproduced experimentally; therefore a field vaccine trial is the only way to determine whether vaccination against *Clostridium botulinum* type C prevents EGS. Half of the horses and ponies on the trial will be vaccinated with the *Clostridium botulinum* type C toxoid vaccine; the other half of the horses and ponies will receive an inactive placebo injection. Comparing the number of EGS cases occurring within the vaccinated group to with the number of EGS cases occurring within the placebo-treated group will show whether or not vaccination significantly reduces the risk of EGS.

What is a placebo injection?

A placebo is an inactive substance containing no medication, used as a control in tests to determine the effectiveness of a medicinal drug/vaccine. In the EGS vaccine trial, the placebo injection will have the same formulation as the vaccine except that it will not contain the active component (the inactivated *Clostridium botulinum* type C toxins).

Who would be administering vaccine or placebo injections during the vaccine trial?

Horses and ponies enrolled in the vaccine trial would remain under the care of the veterinary practice with which they are registered throughout the trial, and we hope that your usual veterinary practice will be able to carry out each visit. Specifically trained EGS vaccine trial veterinary surgeons would also be available to perform health checks and administer vaccines or placebo injections for your horses/ponies if, for any reason, your usual veterinary practice were unable to.

How many veterinary visits are involved in the vaccine trial?

The EGS vaccine trial involves a minimum of 4 veterinary visits during the first year, and a further 2 veterinary visits in the second year. All veterinary visits included in the vaccine trial would be conducted during the normal working hours of the veterinary practice with which you are registered.

Would my horse or pony receive the vaccine or the placebo?

On each premises participating in the EGS vaccine trial, half of the horses and ponies will receive the vaccine and the other half will receive the placebo. Which treatment your horse or pony would receive will be selected at random at the start of the vaccine trial using computer-generated random numbers. To ensure the scientific validity of the EGS vaccine trial, neither you, nor your veterinary surgeon, nor the researchers will be informed of the treatment group which your horse or pony has been selected to join.

When will I find out whether my horse or pony received the vaccine or the placebo?

To ensure that the findings of the EGS vaccine trial are not influenced in any way by the expectations of people taking part, you will be informed of which treatment group your horse or pony was in once the final analysis of results has been performed at the end of the vaccine trial.

Will any details of the vaccine trial treatments be recorded in horse or pony's passport?

Yes – following administration of each vaccine or placebo injection, your veterinary surgeon will record the date and batch number of the injection in the "vaccinations other than equine influenza" section of your horse or pony's passport. At this time point, neither you nor your veterinary surgeon will know whether your horse or pony has received the *Clostridium botulinum* type C toxoid vaccine or the placebo, therefore the Animal Test Certificate number will be recorded in the "name of vaccine" section.

Can my horse or pony have other vaccinations at the same time as vaccine trial treatments?

Wherever possible, administering one of the trial vaccine or placebo injections at the same time as a routine vaccination (including influenza and/or tetanus or Equine Herpes Virus (EHV 1,4)) should be avoided, as it is possible that giving both vaccinations together might alter your horse or pony's immune response to one or both of the vaccines. Allowing a period of two weeks between vaccine trial treatment administration and administration of other vaccinations is recommended (i.e. other vaccinations should be given more than two weeks before or more than two weeks after any trial treatment injection). Where it is not possible to avoid giving the trial treatment within two weeks of other vaccinations, we would ask that your veterinary surgeon administers the other vaccine in a different area (e.g. in the hindquarters or chest, rather than the neck).

My horse or pony has had EGS in the past – can I still take part?

No, unfortunately not. As we do not know how having EGS in the past may influence a horse or pony's immune response to the vaccine, we will not be including any horses or ponies who have recovered from EGS in the vaccine trial.

I don't see my horse or pony every day – can I still take part?

Yes – provided you have someone you can nominate on your behalf to attend veterinary visits and to check your horse or pony every day for the first week following each injection.

My mare is in foal – can I enrol her in the vaccine trial?

No, unfortunately not. As the vaccine has not yet been tested in pregnant mares, we will not be including any mares in foal, or mares with foals at foot.

My horse or pony is needle shy – should I enrol them in the vaccine trial?

We would advise that you discussed this with your veterinary surgeon before deciding whether or not to take part. The EGS vaccine trial involves several injections and blood samples, and there is a possibility that if your horse or pony is already frightened of injections, they may find taking part in the trial stressful.

Why would I have to complete several questionnaires during the vaccine trial?

It is very important that we are able to gather detailed information about the management and health of all enrolled horses and ponies throughout the EGS vaccine trial. The most convenient way for us to collect this vital information is via questionnaires at regular intervals.

Will taking part in the trial affect my horse or pony's insurance cover?

Possibly – in every case, you would have to inform your insurance company **before enrolling your horse or pony** on the EGS vaccine trial. Your insurance company would then inform you of any changes they might make to your existing insurance policy if your horse or pony was enrolled in the trial.

Can I exercise my horse or pony after injections?

Yes – no specific exercise restrictions post-injection with either the vaccine or placebo would be required, and light exercise following injections is acceptable. However, extreme or high intensity exercise should be limited for a period of three days following each vaccine or placebo administration.

I compete my horse or pony – can I still take part?

Yes – however as competition rules of affiliated equestrian organisations can differ, we would advise that you seek clarification of competition rules with the appropriate affiliated equestrian organisation prior to deciding whether or not to participate. Enrolment in the vaccine trial would not affect a horse or pony's eligibility to complete under competition rules of the Fédération Equestre Internationale (FEI), as the FEI have no specific requirements regarding vaccination except for equine influenza, details of which can be found at: http://www.fei.org/fei/horse-health-and-welfare/int-health-requirements/vaccinations
We will be able to provide you with a document detailing your horse or pony's enrolment in the trial to accompany your passport for any required inspections.

I have a racehorse in training – can I still take part?

Yes – racehorses in training will be permitted to race during the vaccine trial, provided that vaccine or placebo injections are administered in compliance with the British Horseracing Authority Rules of Racing. As with other vaccinations, six clear days (starting from the day following injection) must elapse between vaccine administration and race day (as per Rule (B) Schedule 3 Part 1, 10.2 http://rules.britishhorseracing.com/Orders-and-rules&staticID=126400&depth=3). We will be able to provide you with a document detailing your horse's enrolment in the trial to accompany your passport for any required inspections.

- These requirements apply only to races conducted under the British Horseracing Authority Rules of Racing. If you intend to enter, or it is possibly that you might enter, your horse into any overseas race during the vaccine trial, you are advised to seek clarification of racing rules with the appropriate racing authority prior to deciding whether or not to participate.
- If your horse is not in training at the time of enrolment but begins training at some point during the vaccine trial, they would be permitted to race, provided that vaccine or placebo injections are administered in compliance with the British Horseracing Authority Rules of Racing as outlined above.

Are there any risks involved in participating in the vaccine trial?

Local reactions at the site of injection, such as slight swelling, heat or pain, can sometimes occur following intramuscular injections. In previous safety and pilot studies, both the vaccine and placebo have been shown to be safe, with a very small number of horses and ponies showing minor reactions at the site of injection, which did not require any form of treatment. As with any injection, there is always a small risk of injury to people handling the horse or pony and the veterinary surgeon at the time of injection.

What happens if my horse or pony develops signs of EGS during the vaccine trial?

At any point during the EGS field vaccine trial, if you are concerned that your horse or pony may be displaying clinical signs of EGS, you should contact your veterinary practice immediately. Your veterinary surgeon will then perform a clinical examination, any necessary further tests and administer any treatment required. In the case of acute or subacute EGS, a *post mortem* examination would be required to confirm the diagnosis of EGS. Where a diagnosis of chronic EGS is suspected, an additional veterinary examination by one of the specialist equine veterinary surgeons working on the vaccine trial would be required to obtain clinical confirmation of this diagnosis.

Is there any cost involved in participating in the vaccine trial?

Veterinary fees and costs directly related to the EGS vaccine trial, such as the vaccine and placebo injections, veterinary visits and blood test will be covered by the trial. You would however remain responsible for the costs of any routine healthcare, and for the treatment of any condition or injury not directly related to the trial, such as on-going treatment for a long-term condition.

Who can I contact if I have further questions?

If you have any questions, or would like to request any further information, please contact:

Dr Jo Ireland
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Animal Health Trust
Lanwades Park
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Glossary of terms

Term	Definition
Antigen	An antigen is any substance that causes the body's immune system to produce antibodies against it.
Antibody	An antibody is a protein produced by the body's immune system when it detects harmful substances, called antigens. Each type of antibody is unique and defends the body against one specific type of antigen.
Blinding	Also referred to as "masking", is where some of the people involved in a trial or experiment are prevented from knowing certain information that might lead to conscious or subconscious bias on their part, thus invalidating the results. In this study, owners and veterinary surgeons will not be aware of whether each horse or pony is receiving the vaccine or the placebo.
Body condition score	Body condition scoring is a system that uses assessment, visually and by feel, of specific areas of the body to estimate the relative fat cover or "condition" of a horse or pony.
Booster	A booster vaccination is an extra administration of a vaccine after an earlier primary vaccination course, intended to increase immunity against that antigen back to protective levels after it has decreased over time.
Candidate vaccine	This is a specific brand of vaccine that will be assessed in the vaccine trial.
Clinical examination	This refers to any physical examination conducted by a veterinary surgeon in which they examine a horse or pony for any signs of disease or injury.
Clostridium botulinum type C	*Clostridium botulinum* is a species of bacteria that produces several toxins, types A-G. *Clostridium botulinum* type C is the strain of bacteria which produces type C toxins.
Computer-generated random numbers	Using a computer programme to generate a sequence of numbers that lack any specific pattern.
Corticosteroids	A group of drugs, most commonly used for their anti-inflammatory action. In equine medicine, corticosteroids are most commonly used as medication for the treatment of allergic conditions, such as sweet itch and allergic respiratory disorders.
Diagnosteq	Diagnosteq is a laboratory service set up by the Equine Division of Liverpool University's Veterinary School, providing tests for measuring worm burden and advice for equine worm control.
Diagnostic tests	A diagnostic test is any kind of test that a veterinary surgeon may perform to aid in the diagnosis or detection of disease.
Ethical approval	This means that the details of how the EGS vaccine trial will be conducted have been reviewed by a committee with regard to the ethical implications of this research, and approval to conduct this research has been granted.

Exclusion criteria	Exclusion criteria are the standards used to determine whether an owner and their horse/pony may not be allowed to participate in the EGS vaccine trial.
Field vaccination trial	This is a trial of the effectiveness of a vaccine, and a field trial is the veterinary equivalent of a "clinical trial" involving human patients.
Immune response	The body's immune system protects the body from potentially harmful substances by recognising and responding to antigens – this is referred to as the immune response.
Incidental findings	Incidental findings are previously undiagnosed medical conditions or abnormalities that are discovered unintentionally during a veterinary examination, which may or may not be of significance to your horse/pony's health.
Inclusion criteria	Inclusion criteria are the standards required to allow an owner and their horse/pony to participate in the EGS vaccine trial.
Injection site reaction	This is an adverse reaction following injection, at the site of the injection, and may include swelling, heat, pain, abscesses or stiffness in the region of the injection.
Intramuscular injection	Where an injection is administered directly into a muscle. In horses and ponies, the most common sites for intramuscular injection are the neck, the hindquarters and the chest.
Lymph nodes	Lymph nodes are small ball or oval-shaped organs of the immune system, distributed widely throughout the body. They are sometimes incorrectly referred to as the horse/pony's "glands".
Natural immunity	Protection by the immune system acquired by natural exposure to antigens in the horse/pony's environment.
Needle shy	This term may be used to describe a horse/pony that is scared of or resents injections.
Neurotoxins	These are toxins that cause damage to the nervous system.
Noxious agent	A noxious agent is any chemical or biological substance that plays some role in producing the occurrence of a disease.
Peer reviewed veterinary scientific journal	A veterinary journal where any papers submitted must be reviewed by experts in the field before being accepted for publication.
Pilot study	A pilot study is a small-scale preliminary study conducted in order to evaluate feasibility, time, cost, and adverse events to improve upon the study design prior to performance of a full-scale research project.
Pilot field vaccine trial	This refers to the small-scale field vaccine trial that was conducted prior to the full-scale nationwide vaccine trial.
Placebo	A placebo is an inactive substance containing no medication used as a control in an experiment or test to determine the effectiveness of a medicinal drug/vaccine.

Placebo-treated	This is a group of animals or patients receiving the placebo substance.
Post mortem examination	An examination of a body undertaken to determine the cause of death.
Post-treatment observation recording form	This would be the form we would ask you to complete with details of daily inspections of your horse/pony following an injection.
Pre-treatment clinical examination form	This would be the form we would ask your veterinary surgeon to complete with details of his/her health check of your horse/pony prior to administering the vaccine or placebo.
Primary vaccination course	The complete course of vaccinations required to result in a protective immune response.
Randomisation	The process by which horses and ponies are randomly selected to join either the vaccine group or the placebo group.
Routine preventive healthcare	This includes any healthcare measure that you normally provide for your horse/pony, for example influenza ('flu) vaccination, tetanus vaccination, teeth rasping, deworming, supplements and farrier care.
Safety study	A study involving a small number of horses conducted to determine if the candidate vaccine is safe. In the safety study, horses were given 4 doses of the vaccine at 3 week intervals and monitored for any signs of adverse reactions.
Systemic reaction	When an adverse reaction spreads from a limited area of one organ to other organ systems in the body, it's known as a systemic reaction.
Tapeworm antibody levels	Levels of antibodies in the blood stream against the antigens present in tapeworm – these antibody levels can be used provide an estimate of how many tapeworms are present in the horse/pony's body.
Toxico-infectious	Rather than disease being caused by infection with *Clostridium botulinum*, or being caused by consuming *Clostridium botulinum* toxins, it is thought that EGS is caused by *Clostridium botulinum* type C that are already present within the horse/pony's digestive tract which then release their toxins in response to trigger factors – this complex pathway of causing the disease is referred to as a toxico-infection.
Toxoid vaccine	Toxoid vaccines are made from inactivated toxic compounds, rather than the bacteria. The candidate vaccine in this EGS field vaccine trial contains the inactivated *Clostridium botulinum* type C toxins.
Trial study period	The entire time period over which the EGS field vaccine trial will be conducted.

Unique identification number	Your horse or pony would be given an individual identification number when enrolled in the vaccine trial. The first half of this number will code for the premises where your horse/pony is kept and the second half of the number will be unique to your horse/pony. This will allow us to perform randomisation quickly and effectively.
Valid passport	Horse Passports Regulations 2009 mean that it is a legal requirement for owners to have a passport for their horse, pony or donkey. Before this legislation came in to place, some breed society and equestrian organisation passports did not contain all of the information now required by law. For a passport to be "valid" it must contain the correct owner details, horse/pony details and Section IX (the declaration regarding human consumption).
Veterinary health checks	Several veterinary visits will be required at specific time points throughout the vaccine trial and at each visit your veterinary surgeon will perform a health check for your horse/pony. This examination should take approximately 10 minutes and will include: using a weigh tape to estimate your horse/pony's weight; assessment of body condition score; assessment of general demeanour; taking their temperature; listening to heart and lungs and noting heart and respiratory rate; checking lymph nodes; examination for any discharge from the nose or eyes; and asking you questions regarding your horse/pony's recent health, appetite, thirst, urination and faeces.
Veterinary Medicines Directorate	The Veterinary Medicines Directorate (VMD) is an Executive Agency of the Department for Environment, Food and Rural Affairs (Defra). The VMD is responsible for ensuring the safe and effective use of veterinary medicinal products in the UK.

How to perform post-treatment observations for your horse or pony

On the day of injection	▪ **Please remember to ensure that your horse or pony's passport is available at every veterinary visit.**
	▪ You should stand on the same side as the vet, restraining your horse or pony using a head collar. Your vet will scan your horse/pony's neck using a microchip reader, or if your horse/pony is not microchipped, your vet will confirm their identity by comparison with the identification sketch in the passport.
	▪ Your vet will then complete the pre-treatment health check for your horse/pony.
	▪ To administer the vaccine or placebo injection, your vet will pinch the skin next to the treatment site, and inject the horse/pony into the neck muscle approximately two-thirds of the way from the head towards the shoulder (see Figure 1).
	▪ You should make a note of:
	  ▪ which side of the neck your horse/pony receives his/her injection (i.e. on the nearside/left or offside/right of the neck)
	  ▪ the location of the injection site – this will be an area within the coloured triangle illustrated in Figure 2.

How can I identify any injection site reactions?	*Minor reactions at the site of injection such as slight swelling, heat or pain, can sometimes occur following intramuscular injections in horses and ponies. These types of injection site abnormalities were reported in a small number of horses and ponies in the pilot EGS vaccine trial, and all reactions resolved spontaneously without treatment within 1 or 2 days.* Make your first observations, including examination of the injection site, **1 – 3 hours** after each injection is administered and then at approximately 24 hour intervals on subsequent days.
Visual observations of the injection site	Always **compare the injection site to the same area on the opposite side** of the neck (non-injected side). You should be checking for: ▪ any obvious raised lumps or swellings at or near the injection site ▪ a change in the direction of the hair coat at or near the injection site ▪ any other visible abnormalities compared to the other side of the neck
Physical examination of the injection site	Always **compare the injection site to the same area on the opposite side** of the neck (non-injected side). You should be checking for: ▪ any lumps, raised bumps or swellings on or near the injection site when you run your hand over the neck ▪ any areas that feel hot or warm (compared to the opposite side of the neck) on or near the injection site when you run your hand over the neck ▪ pain or discomfort when you run your hand over the injection site (i.e. does the horse/pony react as if it is in discomfort/move away) ▪ any other abnormalities compared to the other (non-injected) side of the neck
How can I identify any other post-injection abnormalities?	Make your first observations of any other post-injection changes to appetite and behaviour **1 – 3 hours** after each injection is administered and then at approximately 24 hour intervals on subsequent days.
Feeding	Make a note of any changes in your horse/pony's appetite. You should be checking: ▪ is your horse/pony eating less than normal or not at all? ▪ is your horse/pony picking at or uninterested in the feed?
Demeanour/behaviour	Make a note of any changes in your horse/pony's behaviour that are not normal. You should be checking: ▪ does your horse/pony appear quieter than usual? ▪ does your horse/pony appear restless?
How do I record my daily observations?	▪ Record your findings daily for one week after each injection, in the relevant boxes on the Post-treatment Observation Recording Form, using the categories defined on the form. Any additional information can be added in the blank boxes provided. ▪ Where no abnormalities are present within the week following injection, please record a score of 0 for each of the categories on the form.

Figure 1: The vet will pinch the skin next to the treatment site, and inject the horse/pony into the neck muscle in the middle of the neck, approximately two thirds of the way from the head towards the shoulder.

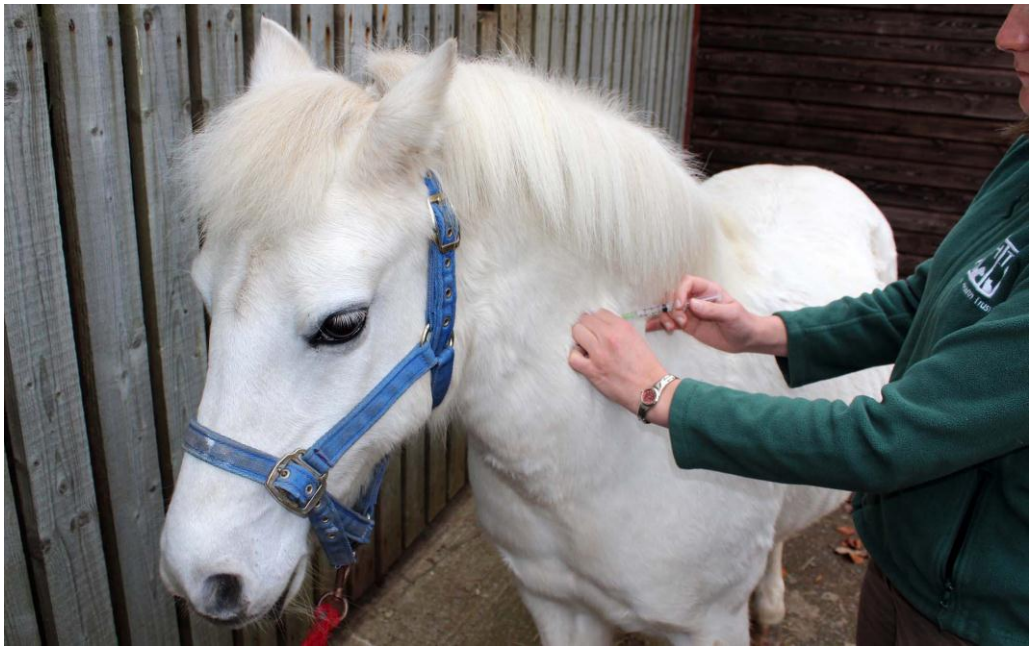
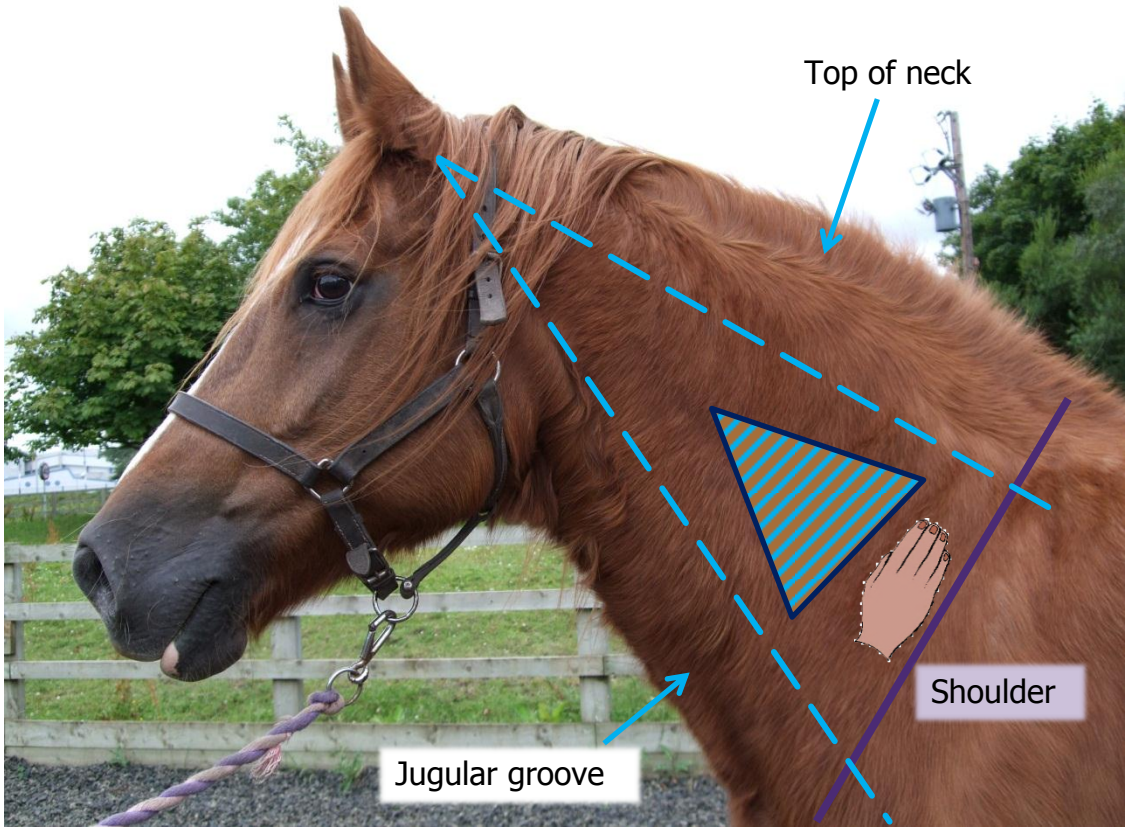


Figure 2: How to identify the injection site area.

Firstly, draw an imaginary line from the base of your horse/pony's ear towards their shoulder (approximately one hand's breadth from the top of the neck) and avoid the area above this line – marked here by the uppermost blue dashed line. Secondly, draw another imaginary line from the base of your horse/pony's ear towards their elbow (approximately one hand's breadth above the groove of the jugular vein) and avoid any areas below this line – marked here by the lower blue dashed line. Finally, identify the outline of your horse/pony's shoulder – shown here in the solid purple line, and move forwards up the neck by one hand's breadth. The injection site should lie in a roughly triangle-shaped area between these lines, approximately two-thirds of the way down the neck from the head – shown here in the coloured triangle.



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Equine Grass Sickness Awareness Group (Facebook)

Equine Grass Sickness Month May

Mrs DM France-Hayhurst Charitable Trust

Miss AM Pilkington Charitable Trust

Sunday Lunch at Strathallan Castle

EB Moller Charitable Trust

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