DEFRA / AHT / BEVA

EQUINE QUARTERLY DISEASE SURVEILLANCE REPORT

Volume 9, No.3: July – September 2013

Highlights in this issue:

- **Equine Influenza in the UK**
- **West Nile Virus in South Europe**
- **Focus article: Pharmacovigilance**

Important note:
The data presented in this report must be interpreted with caution, as there is likely to be some bias in the way that samples are submitted for laboratory testing. For example they are influenced by factors such as owner attitude or financial constraints or are being conducted for routine screening as well as clinical investigation purposes. Consequently these data do not necessarily reflect true disease frequency within the equine population of the United Kingdom.

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Introduction

Welcome to the third quarterly equine disease surveillance report for 2013 produced by the Department for Environment, Food and Rural Affairs (Defra), British Equine Veterinary Association (BEVA) and the Animal Health Trust (AHT). Regular readers will be aware that this report collates equine disease data arising from multiple diagnostic laboratories and veterinary practices throughout the United Kingdom giving a unique insight into equine disease occurrence on a national scale.

National disease occurrence

Equine Influenza (EI)

Equine influenza continues to be of importance within the United Kingdom

Since October 2013, three outbreaks of EI have been diagnosed in the UK.

On the 15th October, the Animal Health Trust confirmed two separate outbreaks of equine influenza in the United Kingdom, one in Lanarkshire, Scotland and the other one in Northamptonshire, England. The affected horse in Lanarkshire was an unvaccinated Thoroughbred-cross mare with clinical signs of fever, mild cough and increased respiratory effort. There were six other non-vaccinated horses on the premises with one of them having arrived on the premises two weeks previously from a dealing yard with clinical signs of fever and nasal discharge, although the horse was not tested for influenza. There second outbreak was confirmed in Northamptonshire, with two affected horses. One was a vaccinated Irish draft mare with clinical signs of depression and mild cough that had arrived in England recently from Ireland. The other animal was an unvaccinated horse that did not showing clinical signs, but tested positive by qPCR on a nasopharyngeal swab. There were three other non-vaccinated horses on the same premises

The last outbreak of EI was confirmed on the 24th October in a Shire Horse stud in Shropshire, England. The eight horses in the stud were reported to show clinical signs of bilateral nasal discharge, mild cough and fever for 5 days

The outbreaks have been reported by the text alert service sponsored by Merial Animal Health, **Tell-Tail**. This free service alerts practitioners to outbreaks of equine influenza in the UK via text message. Equine veterinary practitioners can sign up for this scheme by registering at the following website http://www.merial.co.uk. This service has also been offered to the members of the National Trainers Federation (NTF).

The Horserace Betting Levy Board (HBLB) supports equine influenza surveillance in the UK, including free diagnostic testing for practices that sign up for the AHT's sentinel practice scheme. To register for the scheme and for more information on equine influenza UK vets should visit www.equiflunet.org.uk.

Equine Herpes Virus-1 (EHV-1)

Since October 2014, two outbreaks of EHV-1 has been reported in the UK.

On 15th November 2013, the Animal Health Trust confirmed a presumed case of EHV-1 neurological disease on a private premises with approximately 15 horses in Renfrewshire, Scotland. A 14-year-old Warmblood gelding used for eventing had presented with clinical signs of inco-ordination. The diagnosis of EHV-1 infection was made on the basis of positive qPCR on a nasopharyngeal swab and moderate levels of antibody measured by complement fixation test. The affected horse had several weeks previously travelled to compete in France, sharing the horse box with another horse that had developed clinical signs of fever.

On 22nd November 2013 the Animal Health Trust confirmed a single case of EHV-1 abortion in a vaccinated 4-year-old Thoroughbred mare in East Suffolk, England. The positive diagnosis was made by PCR on fetal tissues. There were three other mares in contact with the aborting mare, all of them vaccinated. The affected mare was isolated and control measures were undertaken in accordance with the HBLB Codes of Practice.

Atypical Myopathy

This condition was first noted in the UK in 1939 and first reported in 1942, although the pathological and epidemiological features of disease did not focus on the environmental toxin hypothesis until 2008. Currently, studies performed in the USA and Europe have pointed a toxic amino acid present in the leaves and seeds of several trees of the genus Acer as the cause of atypical myopathy (AM). This subject will be addressed in a Focus Article in the fourth quarter report that will be published at the end of February 2014.

Since 2004 the University of Liege has been collating data from cases through an epidemiosurveillance network for atypical myopathy that is called Atypical Myopathy Alert Group (AMAG). In2013 up to 28th November, there have been 310 clinical cases that are compatible with diagnoses of atypical myopathy communicated to AMAG. These cases were recorded in Belgium (109 cases), Czech Republic (8 cases), France (81 cases), Germany (37 cases), **Great Britain (40 cases),** Ireland (2cases), Switzerland (11 cases) and The Netherlands (22 cases).

We do encourage veterinary practitioners and owners to collaborate with this network and report cases, either as an owner, via the link :
http://www.myopathieatypique.fr/en/declarer-un-cas/questionnaire-proprietaire/
or as a vet, via the link : https://www.myopathieatypique.fr/espace-professionels/veterinary-form/

International disease occurrence

Equine Influenza

A number of cases of EI were reported throughout Europe and the USA in the third quarter.

On 9th July 2013 the Labor Dr. Böse GmbH confirmed a case of equine influenza in North Rhine-Westphalia. The affected horse was a one year old vaccinated Thoroughbred mare

that showed clinical signs of harsh cough. A positive diagnosis was made by PCR of a nasal swab.

On 19th July 2013 the Swedish Trotting Association confirmed an outbreak of equine influenza in Flyinge, Skåne. The affected horses showed clinical signs of nasal discharge and harsh cough.

On 2nd August 2013 a limited outbreak of clinically mild equine influenza was reported in a Thoroughbred training yard in Turkey by the Turkish Ministry of Food, Agriculture and Livestock. Seven vaccinated horses presented with signs of pyrexia, mucoid nasal discharge and mild cough.

At the beginning of August, equine influenza was also confirmed in Oregon (USA), with 6 affected horses receiving treatment at the College of Veterinary Medicine, Oregon State University.

Equine Herpes Virus-1 (EHV-1)

A case of EHV-1 neurological disease has been reported in a 4-year-old Quarter Horse mare in Contra Costa County, California. The animal, which developed severe neurological signs, had to be euthanased. No other horses were affected at the premises.

Two additional cases were confirmed at a training centre in Landes, France by *Réseau d'Epidémio-Surveillance en Pathologie Equine* (RESPE) in July 2013. The first horse was a three year old vaccinated Thoroughbred that showed clinical signs of ataxia, recumbency, paresis and pyrexia. The positive diagnosis was made by PCR of cerebrospinal fluid. The second positive horse was detected during routine testing of in-contact animals at the same premises, although the horse did not show any clinical signs. Both of the affected horses were imported from the United Kingdom.

West Nile Virus (WNV)

A number of cases of WNV were reported throughout Europe and the USA in the third quarter

Five cases were detected in Greece during this quarter. On 19th July a case of West Nile Virus was reported in Anatoliki, Greece by the OIE based on information from the Ministry Rural Development and Food in Athens. One horse has been subclinically infected and confirmed positive on 17th July 2013 by competitive ELISA. The horse was not treated and control measures were not used. The second case was reported by the OIE based on information from the Ministry Rural Development and Food in Athens, on 29th July in Attiki. One horse has been subclinically infected and confirmed positive on several days after by competitive ELISA. The other three cases were detected in in Dyitiki Ellada region.

In Spain, the Andalucian Ministry of Agriculture, Fisheries and Rural Development confirmed three positive horses during August in Sevilla. No further information was provided.

On 12th Sep 2013, the CESME (National Reference Centre for Exotic Diseases) confirmed three clinical cases in the regions of Emilia Romagna and Lombardy. Monitoring

is carried out in equides by means of periodic examination of sentinel horses, spot checks of resident equides, and verification of suspected cases of WNV. Phylogenetic analyzes carried out on samples of the organs from one of the affected horses made it possible to define the strain as WNV-lineage II.

The number of equine cases of WNV diagnosed in the USA continues to increase significantly, with the national total currently standing at 173 by the end of September, affecting 36 states this year. Most cases have been reported in Montana (27) and Wyoming (18).

Eastern Equine Encephalomyelitis (EEE)

The number of confirmed equine cases of EEE in the USA currently stands at 142. The number of cases by state are as follows: S. Carolina (36), Florida (28), Georgia (20), N. Carolina (12), Mississippi (9), Louisiana (6), Alabama, Maine, Massachusetts (4 apiece), Arkansas, Delaware and New Jersey (3 each), Vermont (2), Connecticut, Kentucky, Maryland, Michigan, New Hampshire, New York, Texas and Virginia (1 each).

Equine ehrlichiosis

On the 12th August 2013 equine ehrlichiosis was reported in the Harelbeke region, Belgium, by the Réseau d'Epidémio-Surveillance en Pathologie Equine (RESPE), based on information obtained from Equi Focus Point Belgium. The 10 year-old mare had presented high fever, anaemia and limb oedema since for two weeks.

Defra/ Animal Health and Veterinary Laboratories Agency (AHVLA) business

The "RED TAPE CHALLENGE"

The Government's first priority is to secure economic recovery and build strong foundations for sustainable economic growth against the backdrop of a rapidly changing world economy.

A central part of the Government's plans in achieving the above goal is to ensure the regulatory environment in which businesses and individuals operate is fit for these challenges.

The Red Tape Challenge (RTC) is intended to tackle the c.21,000 strong stock of existing regulations to help free-up businesses, encourage greater personal responsibility, and create jobs.

The agriculture theme of the RTC opened this summer seeking views on how legislation could be improved.

In reviewing all equine disease regulations, Defra has to challenge the various existing policy areas by assessing them against the following questions

- Could our aims be achieved in a non-regulatory way (e.g. through a voluntary code)?
- Could regulations be reformed, simplified or merged?
- Can we reduce bureaucracy through better implementation?
- Can we make their enforcement less burdensome?
- Should we remove regulations or leave them as they are?

Clearly, some of our Regulations, such as the Infectious Diseases of Horses Order 1987 could be improved to include wider control options for glanders and dourine.

Arguably, some powers / Regulations could be better delivered in a non-regulatory way, for example delisting CEM and EVA as notifiable diseases. **These diseases are not**

notifiable to the EU so we have to ask why we should continue to treat them differently to other Member States. This is also known as ***Gold plating*** - when domestic laws go beyond EU requirements.
This review is at an early stage, and Defra is keen to work with stakeholders in a collaborative and open way. The Department will make a formal announcement early in the new year about next steps, but likely to start as an informal consultation with industry and other interested parties.

Focus article

In this report we are pleased to include a focus article written by Ed Whittle from Elanco Animal Health in pharmacovigilance. The article provides an overview of the importance of pharmacovigilance in ensuring the safety and efficacy of medicinal products.

In addition, it highlights the importance of veterinary practitioners reporting adverse events and lack of efficacy of medicinal drugs. Identification of ineffective vaccines is vital, especially when referred to equine influenza. Reports of vaccine break down are essential to ensure utilization of reference reagents in the selection of viruses for inclusion in vaccines by manufactures.
We reiterate that the views expressed in this focus article are the authors' own and should not be interpreted as official statements of Defra, BEVA or the AHT.

Access to all of the equine disease surveillance reports can be made on a dedicated page on the recently updated Animal Health Trust website at http://www.aht.org.uk/cms-display/DEFRA_AHT_BEVA_equine_reports.html or via the BEVA and Defra websites at http://www.beva.org.uk/news-and-events/news and http://archive.defra.gov.uk/foodfarm/farmanimal/diseases/vetsurveillance/reports/listing.htm, respectively.

We would remind readers and their colleagues that a form is available on the AHT website for registration to receive reports free of charge, via e-mail, on a quarterly basis. The link for this registration form is available via http://www.aht.org.uk/cms-display/equine_disease_registration.html .

Virology Disease Report for the third Quarter of 2013

The results of virological testing for July to September 2013 are summarised in Table 1 and include data relating to Equine Viral Arteritis (EVA), Equine Infectious Anaemia (EIA) and West Nile Virus (WNV) from the Animal Health Veterinary Laboratories Agency (AHVLA), Weybridge. The sample population for the AHVLA is different from that for the other contributing laboratories, as the AHVLA's tests are principally in relation to international trade (EVA and EIA). AHVLA now provides testing for WNV as part of clinical work up of neurological cases on specific request and provided the local regional AHVLA office has been informed.

Table 1: Diagnostic virology sample throughput and positive results for the second quarter of 2013

	Number of Samples Tested	Number Positive	Number of Contributing Laboratories
Serological Tests			
EVA ELISA	628	28	5
EVA VN	96	23	3
AHVLA EVA VN	815	20	1
EHV-1/-4 CF test	875	36	2
EHV-3 VN test	0	0	1
ERV-A/-B CF test	236	7	1
Influenza HI test	296	0	1
EIA (Coggins)	68	0	3
EIA ELISA	247	15	5
AHVLA EIA (Coggins)	1516	0	1
AHVLA WNV (PRNT)	2	0	1
Virus Detection			
EHV-1/-4 PCR	359	18	2
EHV-2/-5 PCR	26	24	1
Influenza NP ELISA	44	0	2
Influenza Directigen	95	0	2
Influenza PCR	129	12	1
AHVLA Influenza PCR	59	0	1
Influenza VI in eggs	16	3	1
EHV VI	109	14	1
EVA VI/PCR	1	0	1
AHVLA EVA VI/PCR	5	0	1
Rotavirus	49	9	9

ELISA = enzyme-linked immunosorbent assay, VN = virus neutralisation, VLA = Animal Health Veterinary Laboratories Agency, CF = complement fixation,

HI = haemagglutination inhibition, Coggins = agar gel immuno diffusion test, PCR = polymerase chain reaction, NP = nucleoprotein,

VI = virus isolation, EVA = equine viral arteritis, EHV = equine herpes virus, ERV = equine rhinitis virus, EIA = equine infectious anaemia
# = Seropositives include vaccinated stallions, * = Diagnosed positive on basis of seroconversion between paired sera ** = Seropositve due to vaccination

Virological Diagnoses for the Second Quarter of 2013

Equine Influenza

The first outbreak was confirmed on 16th July 2013 at a premises consisting of approximately 40 non-vaccinated, non-Thoroughbred horses in Northamptonshire. Twelve animals were reported to have developed typical clinical signs of fever, nasal discharge and coughing within a period of approximately 48 hours.

The second outbreak of EI was confirmed on 24th July 2013 on a private premises in Shropshire with six non-vaccinated, non-Thoroughbred horses and ponies, all of them developed typical clinical signs of mucoid nasal discharge and mild to severe productive coughing.

The first outbreak in September was confirmed on the 2nd September on a premises in Worcestershire with 4 Cob horses affected, showing typical clinical signs of pyrexia, harsh cough and nasal discharge. On the 5th September, a new case in a non-Thoroughbred horse in Warwickshire was detected. This case was linked to the previously reported outbreak in Worcestershire, as horses from both premises had attended the same traveller fair near Redditch.

On the 10th September another outbreak of equine influenza virus infection was confirmed in non-vaccinated, non-Thoroughbred horses in Northamptonshire. Seven of 18 horses on a riding school premises were reported as being affected since 4th September 2013 with signs of fever, inappetance and depression, mucopurulent nasal discharge and severe productive cough being observed. The cases had followed the arrival, several days before the first cases showed signs, of a new horse with mild respiratory signs, which had originated from a market in Warwickshire.

The sixth case was reported on the 13th September in East Yorkshire. The affected pony was reported to have fever, bilateral mucopurulent discharge and severe productive cough. The pony was bought at the York Sales on the 6th September and it was known to have originally travelled from Morpeth, Northumberland.

On the 18th September 2013 a new case was detected in a four-year-old Irish Sports horse in Lincolnshire. The horse had received a first dose of equine influenza vaccine on 5th September 2013, several days prior to being shipped from Ireland with other 20 horses.

The last equine influenza case of this quarter was detected in Lanarkshire, Scotland. The affected non-Thoroughbred horse came from a dealer's yard in West Scotland and presented mild clinical signs of cough, serous nasal discharge and depression.

Equine Herpes Virus-1 respiratory and neurological disease

On 14th August 2013 a case of EHV-1 neurological disease was confirmed on a premises in Oxfordshire. The affected mare presented signs of fever and ataxia. Positive diagnosis was made by post mortem examination and qPCR on several tissues.

On 5th September 2013, a case of concurrent EHV-1 respiratory infection and strangles in a 12-year-old Thoroughbred gelding on a premises in Oxfordshire, England was confirmed. The affected horse, which had been involved in an outbreak of neurological

EHV-1 infection earlier in the year, had recently been moved to other premises in Oxfordshire. The horse was electively euthanased.

Bacteriology Disease Report for the Second Quarter of 2013

A summary of the diagnostic bacteriology testing undertaken by different contributing laboratories is presented in Table 2. For contagious equine metritis (CEM) all 29 HBLB approved laboratories in the UK contributed data.

AHVLA CEMO Data for the period July to September 2013

We are again pleased to include data relating to CEM testing from the Animal Health Veterinary Laboratories Agency (AHVLA), in this quarterly report. The sample population for the AHVLA is different from that for the other contributing laboratories as the AHVLA tests are principally in relation to international trade and/or outbreak investigations.

Strangles

Strangles remains endemic in the UK, especially among parts of the non-Thoroughbred horse population. Diagnoses are confirmed in the UK based on traditional culture of *S. equi* and qPCR on respiratory samples and/or seroconversion using a serological ELISA.

Table 2: Diagnostic bacteriology sample throughput and positive results for the second quarter 2013

	Number of Samples Tested	Number Positive	Number of Contributing Laboratories
CEMO (HBLB)	**938**	**0**	**29**
CEMO (AHVLA)	**682**	**0**	**1**
***Klebsiella pneumoniae*#**	**941[1]**	**2**	**29**
Pseudomonas aeruginosa	**945[1]**	**9**	**29**
Strangles*culture	**1540**	**61**	**20**
Strangles PCR	**1065**	**156**	**4**
Strangles ELISA	**2587**	**580[2]**	**4**
Salmonellosis	**278**	**19**	**17**
MRSA	**646**	**8**	**12**
Clostridium perfringens	**175**	**9**	**8**
***Clostridium difficile* (toxin by ELISA or immunochromatography)**	**152**	**11**	**10**
Borrelia (by ELISA)	**34**	**5**	**1**
Rhodococcus equi culture/PCR	**542**	**4**	**7**
***Lawsonia intracellularis**culture/PCR**	**29**	**2**	**5**

CEMO = contagious equine metritis organism (*Taylorella equigenitalis*); HBLB = HBLB accredited laboratories; # =capsule type 1,2,5; AHVLA = AHVLA reference laboratory**; ***Streptococcus equi* subsp*. equi*; MRSA = methicillin resistant *Staphylococcus aureus.* ** *Lawsonia intracellularis* identified using PCR applied to faeces; [1] reproductive tract samples only; [2] seropositivity may be attributed to disease exposure, vaccination, infection and carrier states.

AHVLA *Salmonella* results

Seven samples were submitted this quarter to the AHVLA and six of them were positive. From the incidents involving strains typed by the AHVLA, the serovars/phagetypes reported were monophasic Typhimurium *variants S.* 4,12:i:- DT193 *(2 samples), S.* 4,5,12:i:- U311 *(1), S.* Anatum *(1) and S.* Enteritidis PT11 *(1) and Typhimurium-DT104b (1). Monophasic Typhimurium DT193 is primarily associated with pigs and U311 with cattle. Salmonella* Enteritidis PT 11 is a hedgehog type and *and S.*Typhimurium *DT104 is likely to be of human origin. S.* Anatum *is often associated with wild birds. For more information from AHVLA about Salmonella in the UK, please visit http://vla.defra.gov.uk/reports/rep_salm_rep11.htm.*

Toxic and Parasitic Disease Report for the Second Quarter of 2013

A summary of diagnostic toxicosis and parasitology testing undertaken by contributing laboratories is presented in Tables 3 and 4, respectively. Results for toxicosis are based on histopathologically confirmed evidence of disease only (where applicable).

Table 3: Diagnostic toxicosis sample throughput and positive results for the second quarter of 2013

	Number of Samples Tested	Number Positive	Number of Contributing Laboratories
Grass Sickness	12	2	5
Hepatic toxicoses	22	2	3
Atypical myopathy	0	0	2*

*Includes contributing laboratories with no cases submitted

Table 4: Diagnostic parasitology sample throughput and positive results for the second quarter of 2013

	Number of Samples Tested	Number Positive	Number of Contributing Laboratories
Endoparasites			
Ascarids	**5096**	**21**	**19**
Cyathostomes	**3190**	**485**	**13**
Dictyocaulus	**1147**	**33**	**11**
Strongyles	**5263**	**1713**	**21**
Tapeworms (ELISA based testing)	**50**	**29**	**8**
Tapeworms (Faecal exam)	**3744**	**119**	**11**
Trichostrongylus	**364**	**10**	**1**
Strongyloides	**4059**	**263**	**18**
Oxyuris equi	**522**	**7**	**5**
Fasciola	**136**	**23**	**3**
Coccidia	**1316**	**16**	**5**
Cryptosporidia	**0**	**0**	**1**
AHVLA *Theileria equi* (CFT)*	**100**	**5**	**1**
AHVLA *Theileria equi* (IFAT)**	**374**	**32**	**1**
AHVLA *Theileria equi* (cELISA)***	**292**	**5**	**1**
AHVLA *Babesia caballi* (CFT)*	**100**	**3**	**1**
AHVLA *Babesia caballi* (IFAT)**	**373**	**18**	**1**
AHVLA *Babesia caballi*(cELISA)***	**292**	**2**	**1**
Ectoparasites			
Mites	**281**	**1**	**17**
Lice	**291**	**0**	**17**
Ringworm	**411**	**69**	**22**
Dermatophilus	**284**	**26**	**17**
Candida	**48**	**0**	**2**

*Complement Fixation Test; CFT suspect/positive samples are tested in IFAT test
**Indirect Fluorescent Antibody Test; ***competitive Enzyme-linked immunosorbent assay; positive cELISA results are not undergoing confirmatory testing

Focus Article: Pharmacovigilance – Beyond the Yellow Form

Ed Whittle, Elanco Animal Health

Most vets will be familiar with the yellow forms found at the back of the NOAH Compendium for reporting adverse events to the Veterinary Medicines Directorate (VMD). These forms are the most visible part of the VMD's Suspected Adverse Reaction Surveillance Scheme (SARSS), and even get a mention in the RCVS Code of Professional Conduct, which states that 'all suspected adverse reactions should be reported using the yellow form' (Royal College of Veterinary Surgeons, 2012). Filling in one of these forms can feel like just another piece of paperwork to add to the "to do" pile, but this underestimates the vital role that pharmacovigilance plays in ensuring the safety and efficacy of medicinal products. In this article I hope to look beyond the yellow form to give an insight into what pharmacovigilance is, and the benefits it brings to vets, animals and owners.

What is Pharmacovigilance?

During the licensing process, drugs are assessed to ensure their safety, efficacy and quality. There are, however, limitations to the trials performed when licensing a new product, including a relatively small sample size which may not be completely representative of the population as a whole, and the relatively short duration of such trials. As a result, despite the rigours of the licensing process, the safety and efficacy profile of a drug may well evolve over time with use. Pharmacovigilance allows the real world use of a product to effectively become a large scale field trial. By recording and analysing adverse events, we are able to identify possible rare adverse events that may not be seen in smaller clinical trials, monitor known reactions (including lack of efficacy), and identify potential risk factors which may promote them. If, after further investigation, these possible associations are confirmed, then the appropriate actions can be taken to mitigate risks, thus maintaining the efficacy and safety of the product.

A great definition of pharmacovigilance can be found below. This neatly sums up the collaborative nature of the process, its relevance to the real world, and the wide reaching benefits that can be achieved.

'Pharmacovigilance is the combined efforts of authorities, industry, the veterinary profession and end-users to evaluate the safety and efficacy of veterinary medicines in practical use situations and to incorporate these findings in product availability and documentation in order to optimise animal health, welfare and public health.' (O'Rourke, 2009)

What counts as an adverse event?

As can be seen from the definition above, everyone involved with the production and use of veterinary medicines, including owners, has a role to play in reporting suspected adverse events. But what counts as an adverse event?

The VMD defines an adverse event as –

'*any observation in an animal, whether or not considered to be product related, that is unfavourable and unintended and that occurs after any use of a veterinary medicine'* (Veterinary Medicines Directorate, 2011).

Adverse events associated with veterinary medicines include reactions in animals which occur after use in accordance with the datasheet (on-label use) or following off-label use,

suspected lack of efficacy after use in accordance with the label, and reactions in humans following exposure to a veterinary medicine or a treated animal.
This is an intentionally broad definition, and captures quite a lot of outcomes in veterinary practice which vets may not consider to be an adverse event, or feel are not worth reporting. For example, a suspected lack of efficacy, such as signs of equine influenza in a horse that is up to date with its vaccines, would count as an adverse event and so should be reported. If suspected lack of efficacy cases are not reported, then how can the product's efficacy be monitored? If adverse events are not reported, then how can we assess whether their incidence is increasing, or linked to other factors? If in doubt, then the case should be reported.

Who should adverse events be reported to?
There are two ways that adverse events can be reported in the UK. The first is to report the adverse event directly to the VMD. This can be achieved either through the yellow forms, or directly via the VMD website - https://www.vmd.defra.gov.uk/adversereactionreporting/.

The second route is to contact the manufacturer[1] of the product directly. Manufacturers have a legal obligation to record any information that they receive about adverse events involving their products and, where appropriate, carry out an investigation. Serious adverse events and human reactions must be sent to the VMD within 15 calendar days of receipt of the case, while non-serious adverse events are reported as part of a document called a Periodic Safety Update Report (PSUR), which are submitted to the Regulatory Authority (either the VMD or the European Medicines Agency (EMA)), on a regular basis, depending on how long the product has been licensed.

It should be noted that a serious adverse event does not just entail death; there are non-fatal serious adverse events. Non-fatal serious adverse events may be life-threatening, may result in significant disability or incapacity, may produce permanent or prolonged signs in the treated animal, or could be a congenital abnormality or birth defect. Examples of such adverse events include anaphylaxis, blindness, immediate collapse lasting longer than 10 minutes, and convulsions or neurological signs occurring within a few hours of administration of a product. Further information can be found within Veterinary Medicines Guidance Note 11 (Veterinary Medicines Directorate, 2011).

Isn't it easier to report cases directly to the regulatory agency?
While reporting a case to the VMD ensures that the case is entered directly into their database, the VMD does not carry out any follow up investigation of the case. The VMD will inform manufacturers of adverse events that have been reported directly to them, but this process takes time and in some cases the reporter's contact details are not passed to the manufacturer. Investigation of a case in a timely manner is often of great importance to determining whether the product was associated with the adverse event or not, known as 'causality'. Without the ability to assess causality accurately, the value of that case for shaping the safety and efficacy profile of the product is vastly reduced. For this reason, reporting the case directly to the manufacturer, who has an obligation to investigate the case where appropriate, and the staff to support this, has major benefits.

[1]Technically, it is the Marketing Authorisation Holder (MAH) who is responsible for recording and reporting suspected adverse events relating to their products to the Regulatory authorities. In many, but not all, cases the MAH is also the manufacturer. For ease of understanding, the term 'manufacturer' is used synonymously for MAN in this document.

A situation where timely investigation is important could be a suspected case of equine influenza (EI) in a horse with up to date 'flu vaccinations. Ideally, samples to confirm whether the horse is suffering from EI should be taken within the first few days of signs been seen. If these are delayed, and a diagnosis is not achieved, then it cannot be determined whether that case represents a lack of efficacy for that vaccine in that horse. As a result an inconclusive causality is likely to be assigned, which limits the value of the case in contributing to the overall picture of the product's efficacy. Of course, in such situations these samples may well have been sent to an OIE reference laboratory and so would also have contributed to the broader surveillance of EI.

While ensuring an accurate assessment of causality is of benefit to developing the safety and efficacy profile of the product, it doesn't necessarily address the fact that an adverse event is not just a record on a system, but has an animal, owner and vet attached. Although adverse events are generally uncommon, manufacturers should be the first port of call for information on adverse events. Manufacturers are well placed to understand whether clinical signs are likely to be associated with product administration, and how to manage such signs. They should be willing to provide technical assistance and support to vets, and owners, at what can be a difficult time.

Finally, for those who are concerned that apparent corporate self interest will prevail, and that reporting adverse events to the manufacturer would be akin to filing them in the bin, it is worth noting that a manufacturer's pharmacovigilance premises, records and documents may be inspected by the VMD at any time. Unannounced inspections can and do take place, and lack of compliance with reporting requirements is an offence. Of course, if you are in any way concerned that a case has not been dealt with adequately, then you may report that case directly to the VMD.

What happens once an adverse event has been reported?

On receipt of a case, the details are entered into a database. This includes the details of the animal, the product involved, concurrently administered products, and a narrative of the adverse event itself. The presenting signs of the adverse event are also coded according to a standard dictionary of terminology; this allows for the signs associated with the adverse event to be analysed. Finally, on the basis of the reported information, each case will have a causality assigned to it. There are five categories - A – probable, B – possible, O1 – inconclusive, O – unclassifiable/unassessable, and N – unlikely.

Cases being input into the pharmacovigilance database are continually monitored by the manufacturer, with serious cases and those involving humans being notified to the VMD within15 calendar days. Any concerns raised can be investigated by reviewing the data contained with the pharmacovigilance database, as well as reviewing literature and carrying out other investigations.

In addition, manufacturers regularly submit Periodic Safety Update Reports (PSURs) to the Regulatory Authorities according to a set timetable for each product. These review all the adverse events received by both the manufacturer and the Regulatory Authorities worldwide over the preceding period, looking for any trends which could indicate a relationship between a product and an adverse event. They also review the number and type of adverse events compared to the amount of product sold, allowing the overall risk-benefit of the product to be monitored on an ongoing basis.

Should a potential link be found between a product and an adverse effect then further investigations can be carried out to define the nature of any potential link. If required, then further action may be taken, ranging from alterations to the product's datasheet, through to withdrawal of the product from sale.

Conclusion
Pharmacovigilance plays a key role in ensuring that the medicines on which vets, animals and owners rely on a daily basis remain safe and effective. Regulatory Authorities, manufacturers, vets and owners all have important roles in ensuring this process works effectively for everyone's benefit.

Grass sickness surveillance data (http://www.equinegrasssickness.co.uk/)

Seven cases of equine grass sickness (EGS) have been reported during the third quarter of 2013 (July – September), of which three occurred in England and one occurred in Scotland. Two of the cases reported from England occurred on the same premises within a three-day period. Location was not reported for the remaining three cases. Only one affected premises had a history of previous EGS cases.

These cases comprised five mares/fillies and one gelding (sex was not reported for the remaining case), with a median age of 5 years (range 2 – 14 years). Affected breeds were Arab crosses (n=3), Welsh breeds (n=2), Cob (n=1) and Connemara cross (n=1).

Two cases were reported to have acute EGS, two were reported to have subacute EGS and two were diagnosed with chronic EGS, of which both were reported to have survived to date. Clinical subtype was not reported for the remaining case. Diagnostic information was only provided for three cases, all of which were diagnosed based on veterinary assessment of clinical signs alone.
It should be noted that the grass sickness surveillance scheme receives data from a wider population in comparison to the data presented in Table 3 and different diagnostic criteria were used.

The nationwide EGS surveillance scheme was established in spring 2008 to facilitate the investigation of changes in geographic distribution and incidence of the disease in Great Britain. Data gathered by this scheme is collated in a strictly confidential database, and will be an invaluable resource in the development of proposed vaccination field trials of a *Clostridium botulinum* type C toxoid vaccine. **Unfortunately, the number of cases reported to the scheme each year is decreasing. Therefore we would encourage both horse owners and veterinary surgeons to report any cases of EGS by contacting Jo Ireland at the Animal Health Trust (email jo.ireland@aht.org.uk).**

Further information is also available at http://www.equinegrasssickness.co.uk/ where questionnaires, collecting data on both affected premises and individual cases, can be viewed and completed online.

Clostridium botulinum type C EGS Vaccine Trial

A pilot field vaccine trial for a candidate *Clostridium botulinum* type C vaccine against equine grass sickness (EGS), commencing in October 2012, has recently been completed. The pilot vaccine trial conducted in Scotland under an Animal Test Certificate obtained from the Veterinary Medicines Directorate (VMD), using a similar protocol similar to that intended for the subsequent nationwide vaccine trial, comprising a placebo-controlled randomised triple-blinded study of 12 month duration. Data analysis is on-going, and findings from the pilot study have already informed modifications to the design and methodology of the forthcoming nationwide EGS vaccine trial, which is due to commence in January 2014.

Report on Post-mortem Examinations for the Second Quarter of 2013

East Anglia

A total of 26 cases were examined including 17 aborted foetuses and two placenta.

Of the aborted foetuses examined, Equine Herpes Virus-1 (EHV-1) was isolated in one case; there were ten cases of umbilical cord torsion, two cases of placentitis and a single case of twin's pregnancy. Trauma origin was suspected in one case and multiple congenital abnormalities were pointed as the cause of abortion in one case. In the last examined foetus, the cause could not be determined.

A single case of foal death was investigated. A four month-old foal died due to multiple rib fracture and subsequent septicaemia.

Four neurological cases were reported. Examination of the first case revealed a traumatic thoracic fracture (T8 and T9) with spinal cord compression. In the second case, multiple rib fractures and severe segmental fracture of thoracic vertebrae with severance of spinal cord were determined as the cause of death.
Two EHV-1 cases were reported this quarter, the first one was primary paralytic herpes with severe hemorrhagic encephalomyelitis and the second one was a recrudescence of a previous neurological case with concurrent S.equi infection and retropharyngeal abscessation.

Four horses were examined following gastrointestinal disease. Two cases presented colitis. One case suffered from severe colon torsion and mucosal compromise. Single cases of ruptured intestine (associated to subsequent peritonitis) and ileal hypertrophy were also reported.

One horse was investigated for acute collapse and sudden death, the post-mortem examination revealed pulmonary oedema and multifocal pulmonary haemorrhages.

Home Counties

Fifteen cases were examined in this quarter.

One foal death was examined this quarter. Post-mortem examination revealed omphalophlebitis and disseminated abscessation.

Six cases of gastrointestinal disease were reported. Two cases of equine grass sickness were identified along with single cases of gastric rupture, large colon volvulus, eosinophilic colitis and ileal hypertrophy.

Two cases of neoplasia were reported this quarter. The post-mortem examination revealed metastatic melanoma and phaeochromocytoma associated to liver rupture respectively.

One musculoskeletal case was examined in which *osteochrondritis dissecans* was diagnosed.

Hepatic lipidosis and laminitis was determined in the last horse examined.

South West
Four cases were examined in this quarter.

Three gastrointestinal cases were reported. Two cases presented hepatic lipidosis and one case a liver tumour that has not been characterized yet.

West Midlands
Six cases were reported in this quarter.

Four gastrointestinal cases were investigated this quarter. Single cases of peritonitis, amyloidosis, caecum torsion and grass sickness were reported in this area.

One musculoskeletal case was reported being a traumatic penetrating joint injury determined in the post-mortem examination.

Last reported examination was a welfare case with no further information.

Scotland
Eight post-mortem examinations were carried out in this quarter.

Five gastrointestinal cases were reported. Single cases of colonic wound breakdown (following surgery), clostridial haemorrhagic enteritis and sand impaction were confirmed. Two cases of gastric rupture were also identified in post-mortem examinations.

One neurological case was reported and post-mortem examination in a head-shaking case revealed trigeminal neuritis.

Three cases of hepatic encephalopathy no associated to ragwort poisoning were also reported.

Northern Ireland
Three post-mortem examinations were carried out in this quarter.

Two gastrointestinal cases were investigated this quarter, septicaemic listeriosis and idiopathic focal eosinophillic enteritis were identified respectively.

One welfare cases was reported in this quarter. A mare was euthanised on human grounds with a history of repiratory illness, although the post-mortem revealed a high intestinal strongyle and cyathostomin burden.

ACKNOWLEDGEMENTS

This report was compiled by the Animal Health Trust.
We are extremely grateful to the following laboratories for contributing data for this report.

Abbey Veterinary Services
Agri-Food and Biosciences Institute of Northern Ireland
Animal Health Trust Diagnostic Laboratory
Animal Health Veterinary Laboratory Agency
Arundel Equine Hospital
Avonvale Veterinary Practice
Axiom Veterinary Laboratory
Beaufort Cottage Laboratories
Biobest Laboratories
Bushy and Willesley (B & W) Equine Group Ltd.
Capital Diagnostics, Scottish Agricultural College
Carmichael Torrance Diagnostic Services
Chine House Veterinary Hospital
Dechra Laboratories
Donnington Veterinary Group
Endell Veterinary Group Equine Hospital
Hampden Veterinary Hospital
Hampton Veterinary Group Laboratory
IDEXX Laboratories
JSC Equine Laboratory
Lab Services Ltd
Liphook Equine Hospital
Minster Equine Veterinary Clinic
Newmarket Equine Hospital
Oakham Veterinary Hospital
The Donkey Sanctuary
The Royal Veterinary College
Three Counties Equine Hospital
Torrance Diamond Diagnostic Services (TDDS)
University of Bristol, Department of Pathology
University of Edinburgh
University of Glasgow
Valley Equine Hospital

All laboratories contributing to this report operate Quality Assurance schemes, which differ between laboratories. However, all contagious equine metritis (CEM) testing reported was accredited by the Horserace Betting Levy Board (HBLB) with the exception of AHVLA, which acts as the reference laboratory.

The Animal Health Trust (AHT) is extremely grateful to the Horserace Betting Levy Board (HBLB), Racehorse Owners Association (ROA) and Thoroughbred Breeders' Association (TBA) for their continued combined contribution to the AHT's Equine Infectious Disease Service.

We would welcome feedback including contributions on focus articles and / or case reports to the following address:

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