ANNEX 3

EU COMMENTS

ON THE PROPOSED CHANGES TO THE

OIE MANUAL OF DIAGNOSTIC TESTS AND VACCINES FOR TERRESTRIAL ANIMALS

PRESENTED FOR COMMENTS IN OCTOBER 2017

EU COMMENTS
On the proposed changes to the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

SUMMARY:

EU COMMENTS
On the proposed changes to the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Glossary

General comments

The EU can in general support the proposed changes to the glossary. A specific comment is provided below.

Specific comments

LINE 251: The EU suggests including reference to the manufacturer's recommendations as regards the required storage temperature, as follows:

"[...] to temperatures above the ~~required~~ storage temperature required according to the manufacturer's recommendations. [...]"

Indeed, it is usually the manufacturer who provides storage and handling instructions, based on the relevant regulatory approval documentation.

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On the proposed changes to the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Chapter 1.1.3.: Transport of biological materials

General comments

The EU can in general support this revised chapter and has a few specific comments.

Specific comments

LINE 46: The words "a section" should be deleted (repetition).

LINES 117-118: The words "international regulations" contain a hyperlink; however the URL will not be visible in the printed version of the Manual. The URL should thus be spelled out in parenthesis after "international regulations". Furthermore, details as to what type of international regulations is meant should be provided (i.e. UN or other).

LINE 122: It is noted that UN 3291 does not appear in table 1. It should preferably be added to the table, or explanations provided as to what it refers to.

LINE 124: There is a comma at the end of the line, after "Category B", however the sentence and paragraph seem to end there (i.e. either some text is missing, or it should be a full stop).

LINE 161: PRRS is perhaps not a good example of "less pathogenic agents", as there are highly pathogenic strains, and in some countries or regions, these predominate.

TABLE 3: Under UN 2900, at the end of the table, SVD and VS are included. However, these have been delisted from the OIE Code in 2015 for several reasons, including their limited morbidity or mortality in animals; they should thus no longer be classified as Category A.

LINE 232: The full stop is missing after "95 kPA".

LINE 242: As URLs may change over time, it would be appropriate to mention also the title of the document, so as to facilitate finding it on the internet in case the URL no longer works.

LINES 247-255: We note that many of the details provided in this section for Category B are not provided for Category A in section 2 above, and suggest including such details, which seems particular relevant for that category.

LINE 258: It would be useful to indicate where these exact details can be found, e.g. by referring to a document available on the internet.

LINE 292: Similarly, it is unclear where this guidance is available (website?).

APPENDIX 1.1.3.1.: We suggest indicating in a chapeau that the definitions provided here are for the purposes of this chapter only.

APPENDIX 1.1.3.2.: In the caption of Fig. 1 and Fig. 3, we suggest indicating the UN numbers (as is done for Fig. 2).

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Chapter 1.1.8.: Principles of veterinary vaccine production

General comments

The EU appreciates OIE's continuous effort to remove requirements for animal testing from the Manual whenever these are no longer necessary or alternatives exist. We thus can in general support the proposed changes to this chapter. A few specific comments are provided below.

In general, we note that the terms "licensing" and "license" is still used in this chapter. With reference to the report of the September 2017 meeting of the Biological Standards Commission (section 8.3.6., p. 15), the EU suggests replacing it with the term "relevant regulatory approval", which should work in all OIE member countries. Indeed, "licensing" or "license" are terms not used in the EU in this context; in the EU the term used is "authorisation".

Specific comments

LINES 392-393: The EU suggests inserting the words "the target animal" before "batch/serial safety test", and "(TABST)" before "in recognition of".

LINES 393-395: The new sentence starting with "*This should be permitted only when* [...]" should be deleted. Indeed, freedom from residual infectivity, virulence or toxicity testing is not tested in the target species (cats, dogs, horses, pigs or sheep), but in laboratory animals (e.g. mice or guinea pigs). Furthermore, this is also not mentioned in the VICH Guideline 50 or 55. However, there is a draft VICH guideline under development addressing these tests.

Instead, the EU suggests inserting the following sentence:

"As stated in VICH Guidelines 50 and 55, the TABST may be waived by the regulatory authority when a sufficient number of production batches have been produced under the control of a seed lot system and found to comply with the test, thus demonstrating consistency of the manufacturing process."

LINE 404: Please add the following at the end of the sentence, for more complete information:
"and, since many years, does not require a general safety test (abnormal toxicity test) in mice or guinea pigs."

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Chapter 2.1.1.: Anthrax

General comments

The EU can support this revised chapter.

Specific comments

None.

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On the proposed changes to the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Chapter 2.1.2.: Aujeszky's disease (infection with Aujeszky's disease virus)

General comments

The EU can in general support this revised chapter and has a few specific comments.

Specific comments

LINES 125-131: Nowadays, only few diagnostic laboratories will still confirm positive amplicons by Southern hybridisation. Indeed, identification by sequencing the amplified product is presumably more often used and should thus be included in the Manual.

LINE 519: Please delete the words "or serial" – we would typically speak of batches in this context; this is also reflected in the title of the section ("Final product batch tests").

LINE 521: The EU does not support use of the term "licensing"; this should be replaced with "the relevant regulatory approval". Reference is made to the report of the September 2017 meeting of the Biological Standards Commission (section 8.3.6., p. 15). Indeed, "licensing" is not a term used in the EU in this context; in the EU the term used is "authorisation".

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Chapter 2.1.9.: Heartwater

General comments

The EU can in general support this revised chapter and has a few specific comments.

Specific comments

LINES 98 and 101-102: The EU queries why the reference to Louw *et al*., 2005 is being deleted. Indeed, it seems relevant for information on the zoonotic potential of *E. ruminantium*. Alternatively, a more recent reference should be added after the newly added information in **Line 101-102**.

LINES 366-369: These statements are rather of a general nature, and not specific to this pathogen. The OIE should consider whether they are necessary here.

LINES 437 and 497: The publication by Cangi *et al*. is now available. Therefore, the word "accepted" can be deleted.

Furthermore, the words "(in press)" can be deleted from the corresponding reference in **LINE 786** in the list of references.

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On the proposed changes to the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Chapter 2.1.16.: Q fever (vaccine section)

General comments

The EU can in general support this revised chapter and has a few specific comments.

Specific comments

LINE 9: As vaccination is not the only control method for Q fever, we suggest replacing the words "are vaccinated" with "can be vaccinated".

LINE 86: It is not clear what is meant by "filled vaccine." Perhaps a different term should be used.

LINE 95: Please delete the words "or serial" – we would typically speak of batches in this context; this is also reflected in the title of the section ("Final product batch tests").

LINE 96: The EU does not support use of the term "licensing"; this should be replaced with "the relevant regulatory approval". Reference is made to the report of the September 2017 meeting of the Biological Standards Commission (section 8.3.6., p. 15). Indeed, "licensing" is not a term used in the EU in this context; in the EU the term used is "authorisation".

LINE 110: We suggest replacing the words "authorisation/registration/licensing" in the title with "regulatory approval". Reference is made to the report of the September 2017 meeting of the Biological Standards Commission (section 8.3.6., p. 15).

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On the proposed changes to the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Chapter 2.1.17.: Rabies (infection with rabies virus)

General comments

The EU can in general support this revised chapter and has a few specific comments.

Specific comments

LINE 1: We note that in the current version of the Manual, the rabies chapter is Chapter 2.1.17., not 2.1.2. (this numbering of the chapter seems to have been changed only on p. 1, not on the other pages of the draft chapter).

LINE 2: The title should be revised, as laboratories do not only need to diagnose rabies virus but all lyssaviruses possibly circulating in the field. This is reflected by section A, which covers several Lyssavirus species.

LINE 8: The comma after "example" should be removed.

LINE 19: We suggest deleting the word "primary", as it is not necessary in this context.

LINE 40: The EU does not support use of the term "license"; this should be replaced with "relevant regulatory approval" (here and throughout the chapter, e.g. **LINES 1001, 1043, 1254, 1270, 1380, 1397**). Reference is made to the report of the September 2017 meeting of the Biological Standards Commission (section 8.3.6., p. 15). Indeed, "licensed" is not a term used in the EU in this context; in the EU the term used is "authorised".

LINE 58: Currently three lyssaviruses are awaiting official classification - additionally Taiwan bat lyssavirus (TWBLV).

LINES 148, 154 and 197: We suggest replacing "impression smear" with "impression or smear".

LINE 156: It should be specified here what is meant by cold acetone, i.e. by inserting "(-20°C)".

LINES 158 and 211: One drop (20ul) of FITC conjugate in practice would be insufficient to cover even a small brain impression. We thus suggest indicating this along the following lines: "use such a quantity of FITC conjugate enough to cover the whole brain impression".

LINE 159: A space is missing between "C" and "in" (should be "37°C in").

LINES 160 and 213: Better not to say "humid box" but rather "humid environment or condition or chamber".

LINE 164: Please replace "recognition" with "identification".

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LINE 184 vs **LINE 218**: Which value is true; CDC technical book for diagnosis of rabies recommends neutral glycerol 9 parts + 1 part of PBS pH8.5.

LINE 189: We would suggest labelling four instead of three microscopic slides.

LINE 203: We suggest the following wording: "[...] cold acetone (-20° C) under the hood for at least 20-60 minutes or fix in a flame by passing the slide 2-3 times".

LINE 211: Please replace the words "working strength" with "working dilution".

LINE 215: For the last washing in PBS, it should be specified that it should be PBS without calcium and magnesium ions.

LINE 312: We suggest amending the title to read: "Virus isolation tests".

LINE 315: With reference to **LINE 174**, we suggest adding "or in all cases human exposure (especially in case of negative results of DFA)".

LINE 323: ATCC recommends Eagle's Minimum Essential Medium (EMEM) – (see https://www.lgcstandards atcc.org/Products/Collections/Cell_Biology_Collections/Cell_Lines/Animal/Mouse/CCL-131.aspx#culturemethod).

LINE 326: Cell culture tests are usually not performed in T25 flasks. Flasks are used for additional passages to increase sensitivity. The use of T25 flasks should thus be transferred to the next sentence.

LINE 334: The concentration should be specified as follows: "20% w/v".

LINE 358: Should be "500 µl" not "ml".

LINES 381-386: In this point there is no volume of inoculum specified, however this should be done, e.g. for suckling (new born) mice 0.01 ml and for older mice it should be up to 0.03ml.

LINE 405: As regards Section 1.3.4. "Polymerase chain reaction (PCR)", for the detection of RNA of lyssaviruses hemi-nested RT-PCR is more reliable/applicable due to the limitation of real-time RT-PCR (non-specific amplification using SybrGreen or others fluorophores; low stability of TaqMan probes and auto fluorescence causing false positive results). Real-time RT-PCR using specific probes (much more specific than the assay with SybrGreen) should be applied for typing of Lyssaviruses. Moreover, the product of the hemi-nested amplification can be used for sequencing and for a phylogenetic study (enough in length in comparison with a short approx. 100bp product obtained in real-time RT-PCR assay).

LINE 410: We would suggest the following, more common wording: "N gene coding viral nucleoprotein" instead of "the nucleocapsid (N) gene".

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LINE 441: Please replace "turn-around" with "turnaround" (typographical error).

LINES 446-449: Does it mean that the serial dilution of RNA stock must be done every time PCR is done, or is it protocol for preparation of PCR positive control? The statements should be revised and perhaps reworded.

LINE 481: PCR controls: NC (reaction mix) as well as PC (known stock of lyssavirus RNA) should be added at each round of PCR.

LINE 483: Reaction can be done in a final volume 25 µl to reduce the amount of reagents needed for the test (it needs validation of course).

LINE 495: We suggest increasing the volume of tested RNA from 1 µl to 2-3 µl /reaction (regardless of the RNA concentration, it also requires validation).

LINE 504: Separation can also be clear when done on 1.5% agarose gel. We this suggest replacing "can be visualised on a 2% agarose gel" with "can be visualised on a 1,5 - 2% agarose gel".
LINE 521: We also recommend decreasing the final volume of the reaction to 25 µl to reduce the amount of reagents needed for the test (it needs validation of course).

LINES 507 and 598: The Manual usually does not mention commercial products (here: "SYBR safe"), unless absolutely necessary. We suggest deleting reference to this commercial product, or at least indicating this is a trademark by adding "™" after SYBR. This comment is also valid for "TRIzol®" (**LINES 415, 598 and 606**).

LINE 582: In our experience instrumentation and equipment should be monitored for satisfactory performance and calibrated at least once every 2-3 years.

LINE 606: We recommend increasing the RNA volume to at least 2 µl.

LINES 693 and 818: What about WHO standard serum in case OIE standard serum of dog origin is not available. Why WHO sera can be use in RFFIT but not in FAVN.

LINE 827: The whole paragraph should be revised for lacking of serum.

LINE 1005: We suggest deleting the words "to this end", as they seem superfluous and make the sentence hard to read.

LINE 1108: Please delete the words "or serial" – we would typically speak of batches in this context; this should also be reflected in the title of the section, that should be consistent with other chapters, i.e. "Final product batch~~/serial~~ tests".

LINE 1110: The EU does not support use of the term "licensing"; this should be replaced with "the relevant regulatory approval". Reference is made to the

report of the September 2017 meeting of the Biological Standards Commission (section 8.3.6., p. 15). Indeed, "licensing" is not a term used in the EU in this context; in the EU the term used is "authorisation".

LINE 1288: Please replace "shall" with "should", as this is the term used for recommendations in OIE standards.

LINE 1332: The word "system" should be plural ("systems").

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Chapter 2.1.19.: Rinderpest (infection with rinderpest virus)

General comments

The EU can in general support this revised chapter and has a few specific comments.

Specific comments

LINE 40 (and 188, 195): We suggest replacing "OIE rinderpest Reference Laboratories" with "FAO/OIE regulated rinderpest holding facilities", in line with the FAO/OIE rinderpest post eradication policy, and for consistency with **LINE 71**.

Similarly, in **LINES 182, 198, 522 and 542**, consistency of wording and spelling should be ensured to avoid confusion, e.g.
- LINE 182: "FAO-OIE-approved Rinderpest Holding Facilities" vs.
- LINE 71: "FAO/OIE regulated rinderpest holding facility" vs.
- LINE 522: "FAO and OIE approved high security laboratories with specific permission to carry out the procedure" vs.
- LINE 542: "FAO-OIE-approved rinderpest holding facility".

LINE 174: "ELISA" should read "cELISA" (typographical error).

LINES 177-178: There is an inconsistency, the abbreviation "RVCM" should be "RPVCM" throughout the chapter for consistency with the abbreviation RPV used for rinderpest virus.

LINE 229: Please replace "multiwall" with "multiwell" (typographical error).

LINE 333: Please insert "RT-" before "PCR assay", as it is indeed a real-time reverse transcription PCR that was described by Carrillo *et al*.

LINE 350: If not ideal, why is RNA purification form spleen mentioned first, or mentioned at all?

LINE 367: What is a "World Reference Laboratory"? Also **LINES 371-373** should be revised to simply refer to "OIE Reference Laboratories" in general (as is done e.g. in **LINES 480-481**).

LINE 482: As the title may be confused with the one of Section 1.2. (**LINE 261**), we suggest inserting the words "Antibody detection by" before "Agar gel immunodiffusion".

LINE 875: What is a "common sense limit"? A wording more appropriate for science based international standards would be preferable.

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Chapter 2.1.24.: West Nile fever

General comments

The EU can in general support this revised chapter and has a few specific comments.

Specific comments

LINE 89-90: As currently there are still no human vaccine commercially available for immediate use, we suggest retaining the part on human vaccines not being available, as follows:

"~~(~~No vaccines are presently available for use in humans, however there is currently a WNV vaccine being used in human clinical trials~~.~~ (NIH, 2015).

TABLE 1: Nested or real-time RT-PCRs are not suited to declare equids free from infection. Indeed, the viremia is short-lived and of low intensity; other matrices are not available prior to movement. Therefore, PCRs are better adapted for the screening of domestic birds prior to movement. This should preferably be specified in the table. The same comment is valid also for isolation in culture.

LINE 133: Sample appropriate for WNV RT-PCR also include the spleen, which is another organ targeted by WNV in birds. Indeed, WNV RNA can be detection from the spleen can be highly sensitive. The spleen could thus be added in the list of samples appropriate for WNV RT-PCR.

LINE 441: Please delete the words "or serial" – we would typically speak of batches in this context; this is also reflected in the title of the section ("Final product batch tests").

LINE 442: The EU does not support use of the term "licensing"; this should be replaced with "the relevant regulatory approval". Reference is made to the report of the September 2017 meeting of the Biological Standards Commission (section 8.3.6., p. 15). Indeed, "licensing" is not a term used in the EU in this context; in the EU the term used is "authorisation".

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Chapter 2.2.5.: Infestation with *Aethina tumida* (small hive beetle)

General comments

The EU thanks the OIE for having taken its previous comments into account and supports this revised chapter.

Specific comments

None.

EU COMMENTS
On the proposed changes to the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Chapter 2.2.6.: Infestation of honey bees with *Tropilaelaps* spp.

General comments

The EU thanks the OIE for having taken its previous comments into account and supports this revised chapter.

Specific comments

None.

EU COMMENTS
On the proposed changes to the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Chapter 2.3.1.: Avian chlamydiosis

General comments

The EU can support this revised chapter.

Specific comments

None.

EU COMMENTS
On the proposed changes to the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Chapter 2.3.2.: Avian infectious bronchitis

General comments

The EU can in general support this revised chapter and has a specific comment.

Specific comments

LINE 702: Please delete the words "or serial" – we would typically speak of batches in this context; this is also reflected in the title of the section ("Final product batch tests").

LINE 703: The EU does not support use of the term "licensing"; this should be replaced with "the relevant regulatory approval". Reference is made to the report of the September 2017 meeting of the Biological Standards Commission (section 8.3.6., p. 15). Indeed, "licensing" is not a term used in the EU in this context; in the EU the term used is "authorisation".

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Chapter 2.3.7.: Duck virus enteritis

General comments

The EU can in general support this revised chapter and has a few specific comments.

Specific comments

LINE 51: Please add the following sentence after "[...] digestive tract mucosa.":
"Specific digestive mucosal lesions may be found in the oral cavity, oesophagus, caeca, rectum and cloaca. Lesions undergo alterations as the disease progresses, from initial macular surface haemorrhages, to yellow-white crusty plaques, then green superficial scabs. Lesions may coalesce and be covered with a diphtheritic membrane."

LINE 134: Further expansion of the PCR protocols would be advantageous; it is unclear as to why a conventional method of detection via PCR is described rather than a real-time quantitative method.

LINE 115: Please remove this sentence: "While this method is not as sensitive as using susceptible day-old ducklings, it is preferable in order to eliminate the need for duckling inoculation." Indeed, as the duckling inoculation method is being removed, that sentence is not necessary.

LINE 347: Please delete the words "or serial" – we would typically speak of batches in this context; this is also reflected in the title of the section ("Final product batch tests").

LINE 348: The EU does not support use of the term "licensing"; this should be replaced with "the relevant regulatory approval". Reference is made to the report of the September 2017 meeting of the Biological Standards Commission (section 8.3.6., p. 15). Indeed, "licensing" is not a term used in the EU in this context; in the EU the term used is "authorisation".

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Chapter 2.3.11.: Fowl typhoid and Pullorum disease

General comments

The EU can in general support this revised chapter and has a few specific comments.

Specific comments

LINE 654: Please delete the words "or serial" – we would typically speak of batches in this context; this is also reflected in the title of the section ("Final product batch tests").

LINE 654: Please delete the words "or serial" – we would typically speak of batches in this context; this is also reflected in the title of the section ("Final product batch tests").

LINE 655: The EU does not support use of the term "licensing"; this should be replaced with "the relevant regulatory approval". Reference is made to the report of the September 2017 meeting of the Biological Standards Commission (section 8.3.6., p. 15). Indeed, "licensing" is not a term used in the EU in this context; in the EU the term used is "authorisation".

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Chapter 2.4.10.: Enzootic bovine leukosis

General comments

The EU can support this revised chapter.

Specific comments

None.

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Chapter 2.4.14.: Malignant catarrhal fever

General comments

The EU can in general support this revised chapter.

We do recognise a nervous component of the clinical signs of the disease, however the changes made in the description of clinical signs suggests this is not the case. They generally occur with clusters of other signs more typical of MCF such as "head and eye".

Specific comments

None.

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On the proposed changes to the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Chapter 2.4.15.: Theileriosis

General comments

The EU can in general support this revised chapter and has a few specific comments.

Specific comments

LINE 80: *T. luwenshuni* has been detected in sheep in the UK associated with clinical signs.
Reference:
Phipps, L.P., Hernández-Triana, L.M., Goharriz, H., Welchman, D. and Johnson, N. Detection of *Theileria luwenshuni* in sheep from Great Britain. Parasites and Vectors (2016) 9:203

LINE 569: Please delete the words "or serial" – we would typically speak of batches in this context; this is also reflected in the title of the section ("Final product batch tests").

LINE 570: The EU does not support use of the term "licensing"; this should be replaced with "the relevant regulatory approval". Reference is made to the report of the September 2017 meeting of the Biological Standards Commission (section 8.3.6., p. 15). Indeed, "licensing" is not a term used in the EU in this context; in the EU the term used is "authorisation".

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Chapter 2.4.16.: Trichomonosis

General comments

The EU can support this revised chapter.

Specific comments

None.

EU COMMENTS
On the proposed changes to the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Chapter 2.4.17.: Animal trypanosomoses (including Tsetse-transmitted, but excluding surra and dourine)

General comments

The EU can support this revised chapter.

Specific comments

None.

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Chapter 2.5.2.: Contagious equine metritis

General comments

The EU can in general support this revised chapter.

However, we do not support Table 1 as currently proposed. Indeed, whilst this table is useful it states that real-time PCR is suitable but not a recommended method as it may need further validation ("++" instead of "+++"). There are of course several PCR methods. Elsewhere in the chapter it states certain advantages of PCR tests over the recommended test (culture) and quotes its successful use in screening and eradication at least. It therefore seems surprising that it is considered less recommended than culture for all purposes.

The table also has a Footnote 1 to agent identification, which states "*A combination of methods applied on the same sample is recommended*." Is it and if so for which purpose? Does it mean that all samples under all circumstances should be tested by more than one method, e.g. culture and IFAT or culture and PCR, or is this a piece of advice that two methods may be more accurate than one – if so is that supported by evidence? Maybe it has value under certain (high risk) circumstances, e.g. testing in-contact animals in an outbreak, or post treatment of a positive horse, but we do not wish to double the testing requirements on every horse by strict interpretation of this footnote.

Furthermore, we note that even though Table 1 includes real-time PCR, molecular diagnostic methods are not described in the chapter. We would suggest including a section on "Molecular testing methods" before point 1.1. "Antibody-based methods", to reflect the importance PCR methods currently play in diagnostic laboratories.

Specific comments

LINE 22: Please insert "Agent identity uses clinical swabs taken from designated genital sites". Indeed, this would explain the sample link between disease and lab techniques.

LINE 70: Please insert "or by contact with fomites typically employed in semen collection or semen used for artificial insemination". Indeed, transmission is not just transmitted by coitus.

LINE 147: Please insert **LINES 16-19** here to identify likely sites that will be swabbed. Indeed, the main text lacks information on where to swab which is quite particular for accurate diagnosis.

LINE 149: Please insert "Designated swabbing sites are usually specified for international trade by the competent authorities."
Indeed, this would provide more information about swabbing, as different countries use or specify different sites.

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LINE 161: Please insert Subtitle "Culture techniques".
Indeed, this section will benefit from dividing up the 3 test types.

Footnote 1: Please replace "is recommended" with "may be advantageous in certain situations". Indeed, this would avoid a requirement to double-test samples.

LINE 235: For reasons of clarity, please insert "to confirm that a culture is *T. equigenitalis*" after "have been developed".

LINE 270: Please replace "1.1 Antibody-based methods" with subtitle "IFAT".
Indeed, this section will benefit from dividing up the 3 test types, and this section is about the IFAT in Table 1.

LINE 279: Please insert subtitle "PCR methods".
Indeed, this section will benefit from dividing up the 3 test types.

LINE 304: Please replace "identify" with "the identification" (grammar).

LINE 312: Please delete the word "yet", as it is unclear whether such vaccines will ever become available or whether research and development are still ongoing to develop such vaccines. Instead, the word "currently" could be used (as is done in other disease chapters for which there are no vaccines).

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Chapter 2.5.4.: Epizootic lymphangitis

General comments

The EU can in general support this revised chapter and has a few specific comments.

Specific comments

LINES 84; 101-110: The EU does not support including descriptions of control measures in the OIE Manual, as this goes beyond its scope. Indeed, control measures are usually included in the OIE Code, and are continuously being deleted from Manual chapters that are being updated. This is the case for example in Chapter 2.5.2., where the section on disease control is proposed for deletion. Therefore, we suggest deleting reference to control in the title of this section, and to delete **LINES 101-110**.

LINE 125: The usual explanation for "PCR" is missing from the list of abbreviations under Table 1.

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Chapter 2.5.11: Glanders and Melioidosis

General comments

The EU can in general support this revised chapter and has a few specific comments.

In general, we support the addition of melioidosis to the chapter, which makes sense due to the relationship with glanders. We note this chapter is primarily about melioidosis in horses, which is appropriate, however since the disease is actually more common in other species it should be highlighted in the text that the emphasis here is on horses.

Specific comments

LINE 8: Please remove "but not contagious". Indeed, the distinction between contagion and infection is rarely made these days and if it is intended to say that the disease is not transmitted by close contact between animals then it should be stated explicitly, however I'm not sure the evidence would support that nor indeed does **LINE 94**.

LINE 8: Please replace "B." with "Burkholderia", as it is the first use of the name in the chapter.

LINE 9: Please insert "sometimes", for the sentence to read "and sometimes resembles glanders." Indeed, the presentation of melioidosis is often more diverse than just glanders-like signs.

LINES 9-11: For reasons of clarity of meaning, please replace "developed" with "evolved"; "has to be" with "is phylogenetically"; and "pathovar" with "a pathovar of B. pseudomallei".

LINE 11: Please insert "This chapter deals with melioidosis in the horse." Indeed, it doesn't deal with other species (see also general EU comment above).

LINE 20: Please replace "were" with "have been" (grammar).

LINE 76: Please replace "denitrificating" with "denitrifying" (grammar).

LINE 80: Please insert "(Rush and Thomas, 2012)" before the full stop. Indeed, this is a useful overview to complement Sprague and Neubauer for other species. (Reference is provided below.)

LINE 82: Please insert ", but more diverse presentations also occur" after "glanders". Indeed, this would avoid confusion that the disease signs are usually the same.
Furthermore, please replace "superacute" with "peracute" (grammar).

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LINES 92-93: Please remove "Conjunctivitis and keratitis are rarely seen", and replace with "Conjunctivitis and keratitis have been reported, though rare."
Indeed, this would avoid implied confusion that conjunctivitis and keratitis are seen in glanders.

LINE 94: Please remove "facilitated", as facilitate isn't applicable here. Furthermore, please remove "abiotic materials" and replace with "materials in the animal's environment." Indeed, abiotic means physical and inorganic, however we should not exclude organic sources, as such material can be contaminated too (e.g. faeces, and soil as well as fomites).

LINE 97: Please replace "regimes" with "regime" (grammar).

LINES 99-100: Please remove this sentence. Indeed, the meaning is unclear. "[...] is established in [...] stables in Europe [...]". Does this mean that there are currently stables in Europe known to be infected with the organism, or that it has been recorded previously in outbreaks and once established is unlikely to go away so current existence is a reasonable presumption? Are we saying there are known equine premises in Europe that are infected? If so it would be helpful to include the rough geography.

LINES 104-105: Please replace the sentence "No reports [...] are available" with "Suitable methods to prevent spread by treatment of manure, waste water or rodent control have not been investigated or reported". Indeed, the meaning is unclear, however we believe the intention is to emphasise that ways to clean the environment are uncertain.

LINE 138: Please insert "or the skin" for the sentence to read "the nasal mucous membranes, sinuses or the skin". Indeed, this would include farcy.

LINE 587: Please insert "Rush, C.M. & Thomas, A.D. (2012). Melioidosis in animals. In: Melioidosis – A century of Observations and Research. Ed: Ketheesan, N. Elsevier BV. pp 312-336."

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Chapter 2.7.4.: Contagious agalactia

General comments

The EU can support this revised chapter.

Specific comments

None.

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On the proposed changes to the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Chapter 2.7.6.: Enzootic abortion of ewes (Ovine chlamydiosis)

General comments

The EU can support this revised chapter.

Specific comments

None.

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On the proposed changes to the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Chapter 2.8.2.: Atrophic rhinitis of swine

General comments

The EU can in general support this revised chapter and has a few specific comments.

In general, the EU is in favour of keeping this existing chapter in the Manual, even if the disease has been delisted from the OIE Code, as it can be useful for laboratories dealing with the respective pathogens.

Specific comments

LINES 358, 368: The EU suggests replacing the word "registration " with "relevant regulatory approval". Reference is made to the report of the September 2017 meeting of the Biological Standards Commission (section 8.3.6., p. 15). Indeed, "registration" is not a term used in the EU in this context; in the EU the term used is "authorisation".

Furthermore, the term "licencing" is misleading (used in the chapter e.g. in **LINES 366, 376, 404, 411**). Indeed, in Europe, the correct term would be "marketing authorisation". We therefore suggest using a more neutral term also in this context, similar to "relevant regulatory approval".

EU COMMENTS
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Chapter 2.8.8.: Swine vesicular disease

General comments

The EU can in general support this revised chapter and has a few specific comments.

Specific comments

LINES 13-15: The EU does not support the addition of these sentences and queries why they were added. Indeed, such information is usually not included in Manual chapters that pertain to diseases that are not listed in the Code, or that have been delisted.

Furthermore, saying that "However, SVD may still circulate unnoticed" and coupling this with "the OIE and its Member Countries continue to require information on the control and diagnosis of SVD" is misleading. Indeed, this could be misunderstood as member countries should still notify occurrence of the disease to the OIE, which is clearly not the case.

Moreover, the main reason the chapter needs to be kept in the Manual after the delisting of SVD from the Code is for differential diagnosis with FMD. This is adequately covered in lines 9 to 12.

Therefore, the EU requests that these sentences be deleted.

LINE 40: The parenthesis "(from 2016)" seems not correct. Indeed, "from 2016" would not be "during the past decade". The character of SVD outbreaks has indeed changed since approx. the year 2000. We thus suggest replacing "2016" with "2000" in the parenthesis.

References:

EFSA (European Food Safety Authority) 2012. Swine Vesicular Disease and Vesicular Stomatitis. EFSA Journal 10(4):2631.

Report of the OIE *ad hoc* group on Swine Vesicular Disease. Paris, 16-17 February 2010.

LINE 345: Only one ELISA is described here, however there are several available commercially. The EU therefore suggests inserting the following at the beginning of the sentence:
"Several kits for antibody detection from pig specimens are commercially available, however in the ELISA developed by [...]".

EU COMMENTS
On the proposed changes to the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Chapter 3.4.: The role of official bodies in the international regulation of veterinary biologicals

General comments

The EU can in general support this revised chapter and has a few specific comments.

Specific comments

LINE 26: The EU suggests replacing the words "registration rules" with "relevant regulatory approvals". Reference is made to the report of the September 2017 meeting of the Biological Standards Commission (section 8.3.6., p. 15). Indeed, "registration" is not a term used in the EU in this context; in the EU the term used is "authorisation".

Furthermore, the term "licence" is misleading (used throughout the chapter, e.g. in **LINES 18, 52, 54, etc.**). Indeed, in Europe, the correct term would be "marketing authorisation". We therefore suggest using a more neutral term also in this context, similar to "relevant regulatory approval".

LINES 133-135: The EU suggests adding a parenthesis at the end of that paragraph, as follows: "(now the European Medicines Agency, EMA)".

EU COMMENTS
On the proposed changes to the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

Chapter 3.7.2.: Minimum requirements for the production and quality control of vaccines

General comments

The EU appreciates OIE's continuous effort to remove requirements for animal testing from the Manual whenever these are no longer necessary or alternatives exist. We thus can in general support the proposed changes to this chapter. A few specific comments are provided below.

Specific comments

Section 2.4.1.2.:

In point 1), the EU suggests deleting the word "in" before "by many regulatory authorities" (syntax error).

Furthermore, in order to provide more complete information in this context, in line with section 2.2. of Chapter 1.1.8., we suggest adding the following after the first sentence of point 1):

"Other regulatory authorities may allow waiving of target animal batch safety tests in line with VICH GL50 and 55."

Moreover, the sentence starting with "Where required, [...]" should be moved to the beginning of point 2). This would allow a clear separation between "not required" and "required" batch or serial safety tests.

In addition, we would request replacing the term "registration" with "relevant regulatory approval", which should work in all OIE member countries. Indeed, "registration" is a term used in only some countries; in the EU, "authorisation" is used instead. Reference is made to the report of the September 2017 meeting of the Biological Standards Commission (section 8.3.6., p. 15). This change should be made throughout the chapter, and eventually throughout the Manual.

Finally, the EU queries whether the last sentence of point 2) is still necessary (starting with "Some authorities do not [...]"), in light of the amended first sentence of point 1) and the additional sentence as suggested above.