

Vaccination recommendations for elephants kept in the EAZA elephant TAG

1 October 2021

Based on historical data on infectious diseases which may have severe clinical impact on elephants kept in EAZA institutions, the vet advisors of the EAZA elephant TAG recommend elephants to be vaccinated against cowpox and *Clostridium tetani*.

As there is no scientific evidence of the efficacy (immune responses) of the sporadically practiced vaccination against multiple *Clostridium spp.*, the decision to use such a vaccine is left to the zoo veterinarian.

More background information is given in the following text.

Cowpox

Cowpox (= Orthopox) virus infections have been reported in both Asian and African elephants. Most cases have occurred in Western Europe. Symptoms may vary from minor lesions to fatal infection. Severe cases have been reported more frequently in Asian elephants than in African elephants, but both species are susceptible.

The European Association of Zoo and Wildlife Veterinarians has produced a fact sheet about cowpox infections in zoo animals, including several references to cowpox infections in elephants (Transmissible Diseases Handbook 2019, see *Annex 1*).

Prevention: preventive vaccination of African and Asian elephants is strongly recommended by the EAZWV and encouraged in the coordinated EAZA breeding programs of both species. The only vaccine available is a Modified Vaccinia Ankara (MVA) vaccine, which is specially produced on request and distributed by the Institut für Infektionsmedizin und Zoonosen, Dr. Robert Fux (Robert.fux@lmu.de), Veterinärstrasse 13, 80539 München, Germany. An example of a batch protocol provided by the producer of the vaccine is given in *Annex 2*. MVA has been used for many years in elephants, rhinos and tapirs without any side effects. Primo-vaccination of keepers or other staff members in contact with vaccinated animals is not required.

In March 2018, the recommendation of the vet advisors for vaccination against cowpox has been endorsed by the EAZA elephant TAG (*Annex 3*):

Vaccination schedule (see also figure 1):

First vaccination (s.c. or i.m.) of 4 ml MVA at the age of 12-16 weeks.

Second vaccination (s.c. or i.m.) of 4 ml MVA 4 weeks after the first injection. The producer of the vaccine advises and offers antibody titer measurement before the vaccination and 3-4 weeks after the second vaccination. In young and untrained elephants this may not be possible, and vaccination should be practiced without titer control.

Booster vaccinations: generally once every 2-3 years, depending on the antibody titer.

Vaccination during pregnancy: following this vaccination advice, elephants should be immune before they become pregnant. There are no sound studies about the possible side effects of vaccination on the fetus. New non-vaccinated imports or elephants with unknown vaccination status should not be bred before they are properly vaccinated.

Remarks: for ordering and using this noncommercial vaccine, a special permit from your official veterinarian is required. Please contact your official veterinarian for further instructions regarding the import of MVA from Germany.

Some countries may impose restrictions regarding the contact between humans (staff, visitors) and elephants for the first two weeks after vaccination. However, there is no recommendation for this

measure and it is not supported by scientific evidence or by the producer. As MVA only replicates once in mammalian tissues, it is safe and developed for use in humans.

References cowpox:

1. Baxby D, Ashton DG, Jones DM, Thomstett LR. 1982. An outbreak of cowpox in captive cheetahs: virological and epidemiological studies. *J Hyg.* 89: 365-372.
2. Chantrey J, Meyer H, Baxby D, Begon M, Bown KJ, Hazel SM, Jones T, Montgomery WI, Bennett M. 1999. Cowpox: reservoir hosts and geographic range. *Epidemiol Infect.* 122: 455-460.
3. Essbauer S, Meyer H. 2007. Genus orthopoxvirus: cowpox virus. In: Mercer AA, Schmidt A, Weber O (eds) *Poxviruses*. Birkhäuser, Basel, Switzerland. pp: 75-88.
4. Eulenberger K, Bernhard A, Nieper H, Hoffman K, Scheller R, Meyer H, Zimmerman P, Essbauer S, Pfeffer M, Kiessling J. 2005. An outbreak of cowpox infection in black rhino (*Diceros bicornis*) at Leipzig Zoo. *Verh ber Erkr Zootiere.* 42:77-85
5. Hentschke J, Meyer H, Wittstatt U, Ochs A, Burkhardt S, Aue A. Kuhpocken bei kanadischen Bibern (*Castor fiber canadensis*) und Katzenbären (*Ailurus fulgens*). 1999. *Tierärztl Umschau.* 54: 311-317.
6. Kurth A, Nitsche A. 2011. Cowpox in Zoo Animals. In: Miller ER, Fowler ME (eds) *Fowler's zoo and wild animal medicine current therapy*, Volume 7. Elsevier, St. Louis, Missouri. pp: 32-37.
7. Kurth A, Straube M, Kuczka A, Dunsche AJ, Meyer H, Nitsche A. 2009. Cowpox virus outbreak in banded mongooses (*Mungos mungo*) and jaguarundis (*Herpailurus yagouaroundi*) with a time-delayed infection to humans. *PLoS One.* 4:e6883.
8. Kurth A, Wibbelt G, Gerber HP, Petschaelis A, Pauli G, Nitsche A. 2008. Rat-to-elephant-to-human transmission of cowpox virus. *Emerg Infect Dis.* 14: 670-671.
9. Marennikova SS, Maltseva NN, Korneeva VI, Garanina NM. 1977. Outbreak of pox disease among carnivora (felidae) and edentata. *J Infect Dis.* 135: 358-366.
10. Martina BE, van Doornum DG, Dorrestein GM, Niesters HG, Stittelaar KJ, Wolters MA, van Bolhuis HG, Osterhaus AD. 2006. Cowpox virus transmission from rats to monkeys, the Netherlands. *Emerg Infect Dis.* 12: 1005-1007.
11. Matz-Rensing K, Ellerbrok H, Ehlers B, Pauli G, Floto A, Alex M, Czerny CP, Kaup FJ. 2006. Fatal poxvirus outbreak in a colony of New World monkeys. *Vet Pathol.* 43: 212-218.
12. Pastoret P-P, Bennett M, Brochier B, Akakpo AJ. 2000. Animals, public health and the example of cowpox. *Rev Sci Tech Off Int Epiz.* 19: 23-32.
13. Pilaski J, Jacoby F. 1993. Die Kuhpocken-Erkrankungen der Zootiere. *Verh ber Erkr Zootiere.* 35: 39-50.
14. Pilaski J, Rosen-Wölff R. 1987. Poxvirus infection in zoo-kept mammals. In: Darai G (ed) *Virus diseases in laboratory and captive animals*. Martinus Nijhoff Publishing, Boston. pp: 83-100.
15. Pilaski J, Schaller K, Matern B, Klöppel G, Mayer H. 1982. Outbreaks of pox among elephants and rhinoceroses. *Verh ber Erkr Zootiere.* 24: 257-265.
16. Pilaski J, Kulka D, Neuschulz N. 1992. outbreak of pox disease in African elephants (*Loxodonta africana*) at the Thuringer Zoopark Erfurt. *Verh ber Erkr Zootiere.* 34: 111-118.
17. Schüppel K-F, Menger S, Eulenberger K, Bernhard A, Pilaski J. 1997. Cowpox infection in alpacas (*Lama glama pacos*). *Verh ber Erkr Zootiere.* 38: 259-265.
18. Wisser J, Pilaski J, Strauss G, Meyer H, Burck G, Truyen U, Rudolph M, Frölich K. 2001. Cowpox virus infection causing stillbirth in an Asian elephant (*Elephas maximus*). *Vet Rec.* 149: 244-246.
19. Zwart P, Gispen R, Peters JC. 1971. Cowpox in okapis (*Okapia johnstoni*) at Rotterdam Zoo. *Br Vet J.* 127: 20-23.

Clostridium tetani

Only a few cases of clinical tetanus in elephants have been described in the literature (Goss 1947, Burke 1975, Fowler et al 2006) or are reported anecdotally for Asian elephants in Southeast Asia. In a preliminary study, measurable titers against tetanus were achieved in Asian elephants vaccinated with a 1 ml dose of monovalent equine tetanus toxoid followed by a booster at 4 weeks. The titers remained elevated for >1 year; however, the appropriate vaccination interval has not yet been determined. Annual vaccination is commonly practiced, although it is likely that the duration of immunity may be longer. In a study in which 9 Asian elephants were involved, Muir et al (2021) demonstrated that the antibody titers in these elephants remained at adequate levels with little fluctuations when 3-5 years intervals were applied. We therefore recommend to adhere to the suggested vaccination regime for horses with booster vaccinations every 2-3 years (see Annex 4 and figure 1).

References tetanus

1. Goss, L.J. 1942. Tetanus in an elephant. *Elephas maximus*. Zoologica NY 27:5–6.
2. Burke, T.J. 1975. Probable tetanus in an Asian elephant. *JZ&WM*, vol 6 – 1 22–24
3. Fowler, M.E. and Mikota, S.K. 2006. Preventive health care and physical examination / Chemical Restraint and General Anesthesia in. In: *Biology, Medicine, and Surgery of Elephants*. 2006. Ed. Fowler & Mikota page 68 / 84.
4. Lindsay, W. A., Wiedner, E., Isaza, R., Townsend, H. G., Boleslawski, M., Lunn, D. P. 2010. Immune responses of Asian elephants (*Elephas maximus*) to commercial tetanus toxoid vaccine. *Vet Immunol Immunopathol* 133 (2-4), 287-289
5. *Transmissible Diseases Handbook*. 2019. Infectious diseases Fact sheet TETANUS (Annex 4)
6. Muir, Y.S.S., Bryant, B., Campbell-Ward, M., Higgins, D.P., 2021. Retrospective anti-tetanus antibody responses of zoo-based Asian elephants (*Elephas maximus*) and rhinoceros (*Rhinocerotidae*). *Developmental & Comparative Immunology* 114, 103841.. doi:10.1016/j.dci.2020.103841

Other *Clostridium spp.*

Several zoos have vaccinated their elephants against multiple-strain *Clostridium spp*, with *Clostridium perfringens* being the major target. Not much is known about the impact of these potential pathogens on the health of elephants. Boonsri et al. describe 2 fatal cases in which *C. perfringens* was involved (Boonsri, 2018). Both cases were associated with EEHV-infection. A study performed in healthy elephants kept in zoos demonstrated the presence of *Clostridium spp*. in 3.5% of the Asian elephants (n=85) and no prevalence in African elephants (n=50) (Scharling, 2021). Preliminary data from necropsy reports revealed 13 cases of *Clostridium spp* involved in the death of Asian elephants (n=226), excluding 5 botulism victims. Of these cases, 5 were attributed to *C. perfringens*, 1 to *C. septicum* and 7 were unclassified *Clostridium spp*. In the same preliminary report, 1 case of *C. perfringens* involvement was found at necropsy of 112 African elephants (Bacciarini, 2001, Hess A, personal communication 2021). Two cases were identified as *C. difficile* (Bojesen A.M. 2006). However, it is not clear from most of the necropsy reports whether *Clostridium spp*. were involved in the primary disease process or just an additional finding. For a long time it was assumed that *Clostridium* was a fatal pathogen in young elephant, but possibly EEHV-HD cases have been wrongly identified as *Clostridium* cases. Now that we look more closely at necropsies, the involvement of *Clostridium* as primary pathogen has become more questionable. Quite severe skin lesions have been anecdotally reported after the use of oil-based vaccines containing multiple *Clostridium spp*. If the zoo vet decides to use a multiple-strain *Clostridium*-vaccine, water-based formulations should be used.

References other *Clostridium* spp.:

1. Boonsri K., Somgird C., Noinafai P., Pringproa K., Janyamethakul T., T., Brown J.L., Tankaeuw P, Srivorakul S., Thitaram C. 2018. Elephant endotheliotropic herpesvirus associated with *Clostridium perfringens* infection in two Asian elephant (*Elephas maximus*) calves. *Journal of Zoo and Wildlife Medicine* 49(1), 178-182.
2. Scharling F.S., Bertelsen M.F., Sós E., Bojesen A.M., 2020. Prevalence of Salmonella species, Clostridium perfringens, and Clostridium difficile in the feces of healthy elephants (*Loxodonta* species and *Elephas maximus*) in Europe. *Journal of Zoo and Wildlife Medicine* 51(4), 752-760.
3. Bacciarini, L. N., Grone, A., Pagan, O., & Frey, J. 2001. *Clostridium perfringens* 2-toxin in an African elephant (*Loxodonta africana*) with ulcerative enteritis. *Veterinary Record*, 149(20), 618–620. doi:10.1136/vr.149.20.618.
4. Bojesen A.M., Olsen K.E.P., Bertelsen M.F. 2006. Fatal enterocolitis in Asian elephants (*Elephas maximus*) caused by *Clostridium difficile*. *Veterinary Microbiology*, 116 (4), 329-335

Annex 1. EAZWV Cowpox fact sheet

Annex 2. MVA-batch protocol provided by the Institut für Infektionsmedizin und Zoonosen (Munich)

Annex 3: Recommendation EAZA elephant TAG regarding MVA vaccination elephants (March 2018)

Annex 4. EAZWV Tetanus fact sheet

Figure 1. Overview of recommended vaccinations

DISEASE (PATHOGEN)	VACCINE NAME	PRODUCER	DOSE /ROUTE OF ADMINISTRATION	AGE OF FIRST VACCINATION	FOLLOW-UP VACCINATIONS
Cowpox (Orthopox virus)	Pox Modified Vaccinia Ankara (MVA), non-commercially produced for zoo mammals	Institut für Infektionsmedizin und Zoonosen, Dr. Robert Fux (Robert.fux@lmu.de), Veterinärstrasse 13, 80539 München, Germany	4 ml i.m./s.c.	3-4 months	First booster after 4 weeks, then every 2-3 years (recommended to measure antibody response)
Tetanus (<i>Clostridium weeks tetani</i>)	Tetanus toxoid 40 LF commercially produced for Equids - EquilisTe - Equip T	For example MSD Zoetis	1 ml i.m.	6 months	First booster after 4 weeks, second primer after 1.5 years, then every 2-3 years

Vet advisors to the EAZA elephant TAG:

Michael Flügger

Thomas Hildebrandt

Imke Lueders

Willem Schaftenaar (coördinator)

Endré Sós