List of Vector Template Changes between Version 1 and Version 2

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| **Version 1 Section (OLD)** | **Version 2 Section (NEW)** | **Changes**(language changes indicated in yellow) |
| **Vaccine Vector Information** |
| 2.1 Name of Vaccines | 2.1 Vector name  |  |
| 2.2 Class/Subtype | 2.2 Vector origin Family/Genus/Species/subtype |  |
| 2.3 Replication | 2.3 Vector replication in humans (replicating or non-replicating) |  |
| 2.4 Formulation | 5.21 Vaccine formulation | Changed section order |
| 2.5 Proposed route of administration | 6.22 Proposed route of administration | Changed section order |
| **Characteristics of the wild type virus from which the vector is derived** |
| N/A | 3.1 Name of wild type virus (common name; Family/Genus/Species/subtype) | Addition of this section in Version 2 |
| N/A | 3.2 What is the natural host for the wild type virus? | Addition of this section in Version 2 |
| 3.1 Any disease caused by wild type, the strength of evidence, severity, and duration of disease for following categories: * Overall
* In immunocompromised
* In neonates, infants, children
* During pregnancy, in unborn
* Are there any other susceptible populations
* Animals
 | 3.7 List any disease manifestations caused by the wild type virus, the strength of evidence, severity, and duration of disease for following categories:* In the healthy natural host
* In healthy human host
* In immunocompromised humans
* In breast milk, human neonates, infants, children
* During pregnancy and in the unborn in humans
* In any other special populations?
 | Changed section order and removed ‘animal’ |
| 3.2 Is there any known evidence of neurological or cardiac involvement of the wild type agent? | N/A | Omission of this section in Version 2 |
| 3.3 What is known about types of human cells infected and the receptors used in humans and animals? | 3.8 What cell types are infected and what receptors are used in the natural host and in humans? | Changed section order |
| 3.4 Does the agent replicate in the nucleus? | 3.5 Does the wild type virus replicate in the nucleus? | Changed section order  |
| 3.5 What is the risk of integration into the human genome? | 3.6 What is the risk of integration into the human genome? | Changed section order |
| 3.6 Does the agent establish a latent or persistent infection? | 3.4 Does the wild type virus establish a latent or persistent infection? | Changed section order |
| 3.7 How does the wild type virus normally transmit? | 3.3 How is the wild type virus normally transmitted? | Changed section order |
| 3.8 What is known about the mechanisms of immunity to the wild type agent? | 3.9 What is known about the mechanisms of immunity to the wild type virus? | Changed section order |
| 3.9 Is there treatment required and readily available for the disease caused by the wild type agent?  | 3.14 Is there treatment available for the disease caused by the wild type virus?  | Changed section order |
| N/A | 3.10 Has disease enhancement been demonstrated with the wild type virus:* In vitro?
* In animal models?
* In human models?
 |  |
| N/A | 3.11 Is DE a possible contributor to the pathogenesis of wild type disease? |  |
| N/A | 3.12 What is the background prevalence of natural immunity to the virus? | Addition of this section in Version 2 |
| N/A | 3.13 Is there any vaccine available for the wild-type virus? If yes,* What populations are immunized?
* What is the background prevalence of artificial immunity?
 | Addition of this section in Version 2 |
| **Characteristics of the vector from which vaccine(s) may be derived** |
| 4.1 What is the basis of attenuation/inactivation of the proposed vaccine vector? | 4.2 What is the basis of attenuation/inactivation of the wild type virus to create the vector? | Changed section order |
| 4.2 What is the risk of reversion to virulence or recombination with wild type or other agents? | 4.5 What is the risk of reversion to virulence or recombination with wild type or other agents? | Changed section order |
| 4.3 Is the vector genetically stable during multiple passages? | N/A | Omission of this section in Version 2 |
| 4.4 What is known about thegenetic stability during in vivoreplication? | 4.6 Is the vector genetically stable in vitro and/or in vivo? | Changed section order |
| 4.5 Will a replication competent agent be formed? | 4.4 Is the vector replication-competent in non-humans species? | Changed section order |
| 4.6 What is the potential for shedding and transmission? | 4.7 What is the potential for shedding and transmission to humans or other species? | Changed section order  |
| N/A | 4.8 Does the vector establish a latent or persistent infection?  | Addition of this section in Version 2 |
| N/A | 4.9 Does the vector replicate in the nucleus? | Addition of this section in Version 2 |
| N/A | 4.10 What is the risk of integration into the human genome? | Addition of this section in Version 2 |
| 4.7 Will the agent survive in the environment? | N/A | Omission of this section in Version 2 |
| 4.8 Is there non-human ‘reservoir’? | N/A | Omission of this section in Version 2 |
| 4.9 Is there any evidence for or against safety during pregnancy?  | N/A | Omission of this section in Version 2 |
| 4.10 Can the vector accommodate multigenic inserts or will several vectors be required for multigenic vaccines? | 4.16 Can the vector accommodate multigenic inserts or will several vectors be required for multigenic vaccines? | Changed section order |
| 4.11 What is known about the effect of pre-existing immunity, on ‘take’, safety or efficacy in any animal model? | 5.19 What is known about the effect of pre-existing immunity, including both natural immunity and repeat administration, on ‘take’, safety or efficacy in any animal model or human studies using this vector? | Changed section order |
| N/A | 4.12 What cell types are infected and what receptors are used in humans?  | Addition of this section in Version 2 |
| N/A | 4.13 What is known about the mechanisms of immunity to the vector? | Addition of this section in Version 2 |
| N/A | 4.14 Has disease enhancement been demonstrated with the vector:* In vitro?
* In animal models?
* In human hosts?
 | Addition of this section in Version 2 |
| N/A | 4.15 Is there antiviral treatment available for disease manifestations caused by the vector?  | Addition of this section in Version 2 |
| **Target Pathogen and Population** |
| N/A | 5.1 What is the target pathogen? | Addition of this section in Version 2 |
| N/A | 5.2 What are the disease manifestations caused by the target pathogen in humans, for the following categories: * In healthy people
* In immunocompromised people
* In neonates, infants, children
* During pregnancy and in the fetus
* In elderly
* In any other special populations
 | Addition of this section in Version 2 |
| N/A | 5.3Briefly, what are the key epidemiologic characteristics of the disease caused by the target pathogen (e.g. incubation period, communicable period*,* route/s of transmission,case fatality rate, transmissibility characteristics such as basic reproductive ratio *(*R0*)* etc.)? | Addition of this section in Version 2 |
| N/A | 5.4 What sections of the population are most affected by the target pathogen (e.g. pediatric, pregnant, lactating women (breast feeding), adult, elderly) | Addition of this section in Version 2 |
| N/A | 5.5 What is known about the correlates of protective immunity to the target pathogen or to the disease? | Addition of this section in Version 2 |
| N/A | 5.6 Please describe any other key information about the target pathogen or population that may inform benefit risk | Addition of this section in Version 2 |
| **Characteristics of vector-based vaccines** |
| N/A | 6.1 What is identity and source of the transgene? | Addition of this section in Version 2 |
| N/A | 6.2 Is the transgene likely to induce immunity to all strains/genotypes of the target pathogen? | Addition of this section in Version 2 |
| N/A | 6.3 Where in the vector genome is the transgene inserted? | Addition of this section in Version 2 |
| N/A | 6.4 Does the insertion of the transgene involve deletion or other rearrangement of any vector genome sequences? | Addition of this section in Version 2 |
| N/A | 6.5 How is the transgene expression controlled (transcriptional promoters, etc.)? | Addition of this section in Version 2 |
| N/A | 6.6 Does insertion or expression of the transgene affect the pathogenicity or phenotype of the vector? | Addition of this section in Version 2 |
| N/A | 6.7 Is the vaccine replication-competent in humans or other species? | Addition of this section in Version 2 |
| N/A | 6.8 What is the risk of reversion to virulence or recombination with wild type or other agents? | Addition of this section in Version 2 |
| N/A | 6.9 Is the vaccine genetically stable in vitro and/or in vivo?  | Addition of this section in Version 2 |
| N/A | 6.10 What is the potential for shedding and transmission to humans or other species?  | Addition of this section in Version 2 |
| N/A | 6.11 Does the vaccine establish a latent or persistent infection? | Addition of this section in Version 2 |
| N/A | 6.12 Does the vaccine replicate in the nucleus? | Addition of this section in Version 2 |
| N/A | 6.13 What is the risk of integration into the human genome? | Addition of this section in Version 2 |
| N/A | 6.14 List any disease manifestations caused by the vaccine in humans, the strength of evidence, severity, and duration of disease for the following categories: * In healthy people
* In immunocompromised people
* In breast milk, neonates, infants, children
* During pregnancy and in the fetus
* In any other special populations
 | Addition of this section in Version 2 |
| N/A | 6.15 What cell types are infected and what receptors are used in humans?  | Addition of this section in Version 2 |
| N/A | 6.16 What is known about the mechanisms of immunity to the vaccine? | Addition of this section in Version 2 |
| N/A | 6.17 Has disease enhancement been demonstrated with the vaccine:* In vitro?
* In animal models?
* In human hosts?
 | Addition of this section in Version 2 |
| N/A | 6.18 What is known about the effect of pre-existing immunity, including both natural immunity and repeat administration of the vector or the vaccine, on ‘take’, safety or efficacy in any animal model or human studies using this vector? | Addition of this section in Version 2 |
| N/A | 6.19 Is the vaccine transmissible in humans or other species (including arthropods) and/or stable in the environment? | Addition of this section in Version 2 |
| N/A | 6.20 Are there antiviral or other treatments available for disease manifestations caused by the vaccine?  | Addition of this section in Version 2 |
| N/A | 6.21 Vaccine formulation | Addition of this section in Version 2 |
| N/A | 6.23 Target populations for the vaccine (e.g pediatric, maternal, adult, elderly etc.) | Addition of this section in Version 2 |
| **Manufacturing** |
| 5.1. Describe the source of the vector (e.g.,isolation, synthesis) | 4.1 Describe the source of the vector (e.g. isolation, synthesis) | Changed section order |
| 5.2 Describe the provenance of the vector including passage history and exposure to animal products.  | N/A | Omission of this section in Version 2 |
| 5.3 Can the vector be produced in an acceptable cell substrate? | N/A | Omission of this section in Version 2 |
| 5.4 Describe the proposed production process. | N/A | Omission of this section in Version 2 |
| 5.5 What are some purity/potential contaminants? | N/A | Omission of this section in Version 2 |
| 5.6 Is there a large-scale manufacturing feasibility? | N/A | Omission of this section in Version 2 |
| 5.7 Are there any IP issues and is there free use of the vector? | N/A | Omission of this section in Version 2 |
| **Toxicology and potency (pharmacology) of the vector** |
| 6.1 What is known about the replication, transmission and pathogenicity in animals? | 7.1 What is known about the replication,transmission and pathogenicity of the vector in and between animals? |  |
| N/A | 7.2. For replicating vectors, has a comparative virulence and viral kinetic study been conducted in permissive and susceptible species? (yes/no) If not, what species would be used for such a study? Is it feasible to conduct such a study? | Addition of this section in Version 2 |
| N/A | 7.3. Does an animal model relevant to assess attenuation exist? | Addition of this section in Version 2 |
| N/A | 7.4. Does an animal model for safety including immuno-compromised animals exist? | Addition of this section in Version 2 |
| N/A | 7.5. Does an animal model for reproductive toxicity exist? | Addition of this section in Version 2 |
| N/A | 7.6. Does an animal model for immunogenicity and efficacy exists? | Addition of this section in Version 2 |
| N/A | 7.7 Does an animal model for antibody enhanced disease or immune complex disease exist? | Addition of this section in Version 2 |
| 6.7 What is known about biodistribution? | 7.8 What is known about biodistribution in animal models or in humans? |  |
| 6.8 Have neurovirulence studies been conducted? | N/A | Omission of this section in Version 2 |
| 6.9. What is the evidence that the vaccines will generate a beneficialimmune response in:* Rodent?
* Non-rodent?
 | 7.9 What is the evidence that vector derived vaccines will generate a beneficial immune response in:* Small animal models?
* Nonhuman primates (NHP)?
* Human?
 | Changed section order |
| 6.10 Have challenge or efficacy studies been conducted with: | 7.10 Have challenge or efficacy studies been conducted with:  | Changed section order |
| N/A | 7.11Have studies been done simultaneously or sequentially administering more than one vector with different transgenes? Is there evidence for interaction/ interference? |  |
| **Previous Human Use** |
| 7.1. Has the vector already been used for targeting the disease of vector origin? | N/A | Omission of this section in Version 2 |
| 7.2 What is known about the replication, transmission and pathogenicity of the vector in: | 4.3 What is known about the replication, transmission and pathogenicity of the vector in humans in the following categories:  | Changed section order |
| 7.3. Is there any previous human experience with a similar vector including in HIV+ (safety and immunogenicity records)? | 4.11 Is there any previous human experience with this or a similar vector (safety and immunogenicity records)? | Changed section order and some wording |
| 7.4 Is there any previous human experience with present vector including in HIV+ (safety and immunogenicity records)? |
| 7.5. What is known about the effect of pre-existing immunity on ‘take’, safety or efficacy in any human studies with this or different insert? | 5.19 What is known about the effect of pre-existing immunity, including both natural immunity and repeat administration, on ‘take’, safety or efficacy in any animal model or human studies using this vector? | Changed section order |
| 7.6. Name some other non-HIV vaccines using same vector and describe some of the public healthconsiderations. | N/A | Omission of this section in Version 2 |
| **Overall Risk Assessment** |
| N/A | 9.1. Please summarize key safety issues of concern identified to date, if any: * How should they be addressed going forward:
 | Addition of this section in Version 2 |
| 8.1 What is the potential for causing serious unwanted effects and toxicities in: * Other susceptible populations?
 | 9.2 What is the potential for causing serious unwanted effects and toxicities in:* In any other special populations?
 | Changed section order |
| 8.2. What is the risk of neurotoxicity/neuroinvasion or cardiac effects? | N/A | Omission of this section in Version 2 |
| 8.3. What is the potential for shedding and transmission in risk groups? | 9.3 What is the potential for shedding and transmission in risk groups? | Changed section order |
| 8.4. What is the risk of adventitious agent (including TSE) contamination? | N/A | Omission of this section in Version 2 |
| 8.5. Can the vector be manufactured at scale in an acceptable process? | N/A | Omission of this section in Version 2 |
| 8.6. Can virulence, attenuation and toxicity be adequately assessed in preclinical models? | N/A | Omission of this section in Version 2 |
| 8.7. Rate the evidence that a beneficial response will be obtained in humans. | N/A | Omission of this section in Version 2 |
| **Adverse Effect Assessment** |
| 9.1. Describe spontaneous adverse effects observed to date and whether related or unrelated. | N/A | Omission of this section in Version 2 |
| 9.2 Describe the reactogenicity  | N/A | Omission of this section in Version 2 |
| N/A | 8.1 Approximately how many humans have received this viral vector vaccine to date? If variants of the vector, please list separately.  | Addition of this section in Version 2 |
|  | 8.2. Method(s) used for safety monitoring:* Spontaneous reports/ passive surveillance
* Diary
* Other active surveillance
 |  |
| N/A | 8.3. What criteria was used for grading the AE’s? * 2007 US FDA Guidance for Industry Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials
* If no criteria were used for grading, or if other metrics were employed, please describe:
 | Addition of this section in Version 2 |
| N/A | 8.4. List and provide frequency of any related or possibly related serious\* AE’s observed: (\*see Instructions): | Addition of this section in Version 2 |
| N/A | 8.5. List and provide frequency of any serious, unexpected AE: | Addition of this section in Version 2 |
| N/A | 8.6. List and provide frequency of any serious, unexpected statistically significantly increased AE or lab abnormality in vaccinee vs. control group:* Describe the control group
 | Addition of this section in Version 2 |
| N/A | 8.7. List and provide frequency of Adverse Events of Special Interest | Addition of this section in Version 2 |
| N/A | 8.8. Did Data Safety Monitoring Board (DSMB) or its equivalent oversee the study?* Did it identify any safety issue of concerns?
* If so describe:
 | Addition of this section in Version 2 |
| 10.1. What is the average Tissue Culture Infections Dose per millimeter (TCID/ml)? | N/A | Omission of this section in Version 2 |
| 10.2. What is the highest TCID/ml that can be used before cell toxicity? | N/A | Omission of this section in Version 2 |
| 10.3. Are different demographics affected differently? | N/A | Omission of this section in Version 2 |
| 10.4 Are there age related differences of dosage?  | N/A | Omission of this section in Version 2 |
| Any Other Information |
| N/A | Blank | Addition of this section in Version 2 |