Brighton Collaboration Benefit-Risk Assessment of Vaccines by Technology (BRAVATO) Working Group
Standardized Template for Collection of Key Information for Benefit-Risk Assessment of Protein Vaccines

Introduction:

The Brighton Collaboration formed the Viral Vector Vaccines Safety Working Group (V3SWG) in 2008 to enhance safety assessments for viral vector vaccines, enabling greater public trust. The Working Group developed a standardized template to evaluate benefit-risk considerations, facilitating clear communication among stakeholders. This template has evolved over time, informed by its use in assessing vaccines like those for Ebola, and is endorsed by the WHO. Additionally, the template approach has been modified to include other types vaccines such as live-attenuated, inactivated, and recombinant protein vaccines. The templates focus on the characteristics of wild-type viruses, viral vectors, and recombinant vaccines, with sections addressing toxicology, adverse effects, and overall safety. The V3WSG has recently been renamed to the Benefit-Risk Assessment of VAccines by TechnolOgy (BRAVATO) Working Group to reflect its expanded role in development of templates for additional vaccine platforms, namely nucleic acid based, live attenuated, inactivated, and protein based vaccines. The latest version of the template can be accessed on https://brightoncollaboration.us/bravato/, ensures transparency, comparability, and stakeholder collaboration for vaccine safety.

Note: This template is for viewing purposes only. Vaccine developers interested in completing the relevant templates for their vaccine platform or candidate and collaborating with BRAVATO should contact the coordinator at bc-coordinator@taskforce.org. The coordinator will provide an introduction and link to the digital tool for template completion.

Brighton Collaboration Benefit-Risk Assessment of Vaccines by Technology (BRAVATO) Working Group Standardized Template for Collection of Key Information for Benefit-Risk Assessment of Protein Vaccines		
1. Authorship	**Information**	
1.1 Author(s) and affiliation(s)		
1.2 Date completed/updated		
2. Basic Vaccine Information	**Information**	**Comments/Concerns**
2.1 Vaccine name		
2.2 Protein type (e.g., molecular clamp, virus-like particle, peptide) and any special characteristics		
2.3 Type of heterologous expression system used for antigen production		
2.4 Final vaccine formulation components that may impact delivery into cells, stability, and safety:		
• Antigen(s)		
• Adjuvants		
• Stabilizers		
• Preservatives		
• Surfactants		
• Diluents		
• Buffers		
• Lipids (in lipid nanoparticles)		
• Emulsifying agents		
• Other Excipients		
2.5 Route and method of delivery		
3. Target Pathogen and Population for the Vaccine	**Information**	**Comments/Concerns**
3.1 What is the target pathogen for the vaccine?		
3.2 What are the disease manifestations caused by the target pathogen in humans, for the following categories:		
• Healthy people		

• Immunocompromised people		
• Neonates, infants, children		
• During pregnancy and in the fetus		
• Elderly		
• Any other special populations		
3.3 Briefly, what are the key epidemiologic characteristics of the disease caused by the target pathogen:		
• Incubation Period		
• Communicable period		
• Route/s of transmission		
• Case fatality rate		
• Reproductive Number (R0)		
• Stability of the virus		
• Other information		
3.4 What sections of the population are most affected by the target pathogen?		
3.5 What is known about the immune responses, duration, and potential correlates of protective immunity to the target pathogen or to the disease?		
3.6 Please describe any other key information about the target pathogen or population that may inform benefit-risk		
4. Characteristics of Antigen	**Information**	**Comments/ Concerns**
4.1 Is the vaccine likely to induce immunity to all strains/genotypes of the target pathogen?		
• What is the evidence?		
4.2 What is known about the immune response to the vaccine in animals and/or humans (binding, functional, and neutralizing antibody, B-cell, T-cell memory, etc.)?		
4.3 Is there homology in the sequence of the vaccine antigen and human proteins?		
5. Adjuvant (if applicable)	**Information**	**Comments/ Concerns**
5.1 Describe the type of adjuvant, if it has been tested in humans, whether novel or commercialized, and if applicable, what other vaccines (preventive and therapeutic)		

are formulated with this adjuvant		
• What is the name of the adjuvant?		
• Describe the type or classification of this adjuvant?		
• Has the adjuvant been tested in human clinical trials?		
5.2 What is the evidence that an adjuvant improves/boosts/enhances the immune response?		
5.3 What is the mechanism of action of the adjuvant (if known)?		
5.4 How is the adjuvant formulated with the antigen?		
5.5 How might the adjuvant impact the safety profile of the vaccine?		
5.6 Summarize the safety findings (preclinical and clinical) with the adjuvant, formulated with any antigen		
6. Delivery and Administration	**Information**	**Comments/ Concerns**
6.1 How might the vaccine formulation (antigen and adjuvant already formulated in the same vial or combined prior to administration) impact the safety profile of the vaccine?		
6.2 If the vaccine is part of a heterologous prime-boost regimen, describe the regimen that this vaccine is a part of and the possible impact on safety		
6.3 Describe how components of the vaccine formulation that facilitate stability and delivery into cells (Section 2.5) may impact the safety profile of the vaccine		
6.4 Describe how the mode of vaccine delivery may impact safety (e.g., intramuscular by needle injection, microneedles, intranasal, oral)		
* Stability is considered here in the context of any relevant intrinsic characteristic of the vaccine deemed important for safety purpose.		
7. Toxicology and Nonclinical of the Vaccine	**Information**	**Comments/ Concerns**
7.1 What is known about biodistribution of the antigen in its final formulation and mode of administration in animal models?		
7.2 How long does the vaccine antigen persist in vivo (may specify in tissue/serum; proximal/distal to site of administration)?		
7.3 What is the possible risk of autoimmunity or a harmful immune response?		
7.4 Summarize the preclinical safety data that support the use of this product in humans including any related information from similar products		

7.5 Summarize the preclinical immunogenicity and efficacy data that support the use of this product in humans including any related information from similar products		
7.6 What is the evidence of disease enhancement or absence thereof *in vitro* or in animal models?		
7.7 Would the vaccine in its final formulation have any impact on innate immunity?		
• If so, what are the implications for benefit-risk in animal models and small non-human primates		
8. Human Efficacy and Other Important Information	**Information**	**Comments/ Concerns**
8.1 What is the evidence that the vaccine would generate a protective immune response in humans (e.g., natural history, passive immunization, animal challenge studies)?		
8.2 Describe other key information that may impact benefit-risk		
8.3 If there are multiple strains of the pathogen, can the vaccine protect against multiple strains or serotypes?		
9. Adverse Event (AE) Assessment of the Vaccine Platform (*see Instructions):	**Information**	**Comments/ Concerns**
9.1 Approximately how many humans have received this vaccine to date?		
• If variants of the vaccine platform, please list separately.		
9.2 Method(s) used for safety monitoring:		
• Spontaneous reports/passive surveillance	Yes/No	If yes, describe method:
• Diary	Yes/No	If yes, number of days:
• Other active surveillance	Yes/No	If yes, describe method (e.g., LTFU) and list the AEs solicited:
9.3 What criteria were used for grading the AEs?		
• If no criteria were used for grading, or if other metrics were employed, please describe:		
9.4 List and provide frequency of any or possibly related serious* AEs and well as any severe expected or unexpected AEs observed: (*see Instructions):		
9.5 List and provide frequency of any serious, unexpected significantly increased		

AE or lab abnormality in vaccine vs. control groups:		
• Describe the control group		
9.6. List and provide frequency of Adverse Events of Special Interest		
9.7 What is the evidence of disease enhancement (if any) in humans?		
9.8 Did a Data Safety Monitoring Board (DSMB) or its equivalent oversee the study?	Yes/No	
• Did it identify any safety issue of concern?	Yes/No	
• If so describe:		
10. Overall Risk Assessment	**Information**	**Comments/ Concerns**
10.1 Please summarize key safety issues of concern identified to date, and how should they be addressed going forward		
10.2 What is the potential for causing serious unwanted effects and toxicities in:	**Describe the toxicities**	**Please rate risk as: none, minimal, low, moderate, high, or unknown**
• Healthy humans?		
• Immunocompromised humans?		
• Breast milk, human neonates, infants, children?		
• Pregnancy and in the fetus in humans?		
• Elderly?		
• Other special populations (e.g., institutionalized population, individuals with associated chronic comorbidity)?		
References	**Information**	
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2.		
3.		
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