

Standardized Template Revisions

The Brighton Collaboration (www.brightoncollaboration.us) was launched in 2000 to improve the science of vaccine safety (1). The Brighton Collaboration formed the Viral Vector Vaccines Safety Working Group (V3SWG) in October 2008 to improve our ability to anticipate potential safety issues and meaningfully assess or interpret safety data, thereby facilitating greater public acceptance when a viral vector vaccine is licensed (2). Chief among the goals of the V3SWG has been the development of a standardized template describing the key characteristics of novel viral vaccine vectors, to facilitate the scientific discourse among key stakeholders and increase the transparency and comparability of information. In 2020, spurred by the SARS-COV-2 pandemic, the mission of the V3SWG was expanded to include templates for other vaccine platforms including nucleic acid, protein, inactivated whole virus, and live attenuated viral vaccines. To reflect this expanded mission, V3SWG was renamed to the Benefit-Risk Assessment of VAccines by TechnoOgy (BRAVATO) Working Group (3).

Development of standardized templates is an evolving process and has to date resulted in four distinct versions of the viral vector vaccine template. To distinguish template versions now and in the future, we use integers to indicate major version changes and decimals to indicate incremental updates, as in software nomenclature. Currently four versions of the templates exist, detailed below. The first three versions applied only to the Viral Vector Template as the others had not been created yet.

v1.0

In 2015, the V3SWG published the v1.0 of the vector template, completed with a description of the yellow fever 17D vaccine vector (4-5), which has been used for construction of recombinant vaccines for Japanese encephalitis (6) and Dengue fever (7). v1.0 of the template was also used to describe a vesicular stomatitis virus (VSV) based vector (8) and a VSV-based Ebola vaccine, rVSVΔG-ZEBOV-GP (9), which was used successfully in a ring vaccination trial in Guinea (10).

v2.0

Experience accumulated during completion of v1.0 of the template revealed that modifications to the template could improve its utility. Fundamental to the template revision was the recognition that a thorough understanding of safety issues associated with vectored vaccine requires a clear understanding of the characteristics of the wild type virus from which the vector is derived, the vector itself, and the vaccine(s) constructed using the vector platform. Depending on the vector or vaccine(s) under consideration, each of these components may exhibit different biological properties; therefore the generic template is constructed to embrace a broad spectrum of possibilities. v2.0 of the template thus contains separate sections devoted to each of the components: wild type virus, the vector, and vaccine(s) based on the vector. The revised template retains a focus on the vector. Because multiple vaccines with different properties may be constructed based on a single vector, the vaccine(s) section of the template may contain some generalities while the vector section (and the wild type virus section) are more specific.

v2.0 of the template revision also deletes two sections from the original template, specifically “Manufacturing” and “Previous Human Use”. The rationale for these changes is that manufacturing is a post-licensing issue beyond the scope of the template, and relevant issues associated with previous human use are incorporated into other sections of the revised template.

Lastly, the sections “Adverse Event Assessment of the Vector” and “Overall Risk Assessment of the Vector” have been updated to comprise a broad assessment of adverse events and overall risk consistent with existing tools for making these assessments.

v2.0 of the template was used to describe an Adenovirus type 4 vector (submitted). v2.0 has also been used to describe an MVA vector (MVA-BN), an Adenovirus 26 vector, and a vaccine regimen combining both adenovirus and MVA vectored Ebola antigens (personal communication).

V3.0

Version 3.0 of the template expands the original viral-vector-specific format to encompass additional vaccine platforms, including viral-vector, nucleic acid, protein, inactivated whole virus, and live-attenuated viral vaccines.

For the viral-vector template specifically, the revisions broaden its scope from a vector-centric focus to a “dual-use” approach, allowing it to describe either a viral vector alone or a vectored vaccine. This expanded functionality is achieved by dividing the template into two distinct parts:

- Part I: Viral Vector
- Part II: Vaccine

Each part includes dedicated sections on Toxicity and Potency, Adverse Effects, and Overall Assessment to ensure comprehensive evaluation. Additionally, Part II, which addresses vaccines, now features a new section on the Target Pathogen.

Numerous incremental refinements have also been made to harmonize the viral-vector template with newly developed templates for other vaccine platforms.

V4.0

v4.0 of the templates is a structural update that reorganizes the existing templates without altering its content. For questions that were previously vague, we have expanded them with sub-questions to guide developers on the specific type of information required. Additionally, template sections have been slightly reworded and reorganized to ensure consistency across other platform-specific templates.

References:

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