Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Vaccine 39 (2021) 3050–3052

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Commentary

The Brighton Collaboration standardized templates for collection of key information for benefit-risk assessment of vaccines by technology (BRAVATO; formerly V3SWG)

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The devastating COVID-19 disease pandemic has led to an unprecedented surge in research and development for safe and effective vaccines against its causal pathogen, the SARS-CoV-2 coronavirus - widely seen as THE best long term solution [30]. As of Oct.26, 2020, 249 COVID-19 vaccines are currently under development, 51 of which are in clinical trials [1]. The candidate vaccines are being developed using a wide range of both established and novel technologies. Established technologies include those that have been used previously for the development of human vaccines and include inactivated whole virus, live-attenuated virus, or immunogenic viral proteins produced by recombinant DNA technology. Novel technologies include platforms for which few (e.g., viral vectored) or no [e.g., nucleic acid (RNA and DNA) licensed human vaccines exist. Several vaccines using these novel technologies are among the most advanced of the COVID-19 vaccine candidates, already in Phase 2 or 3 trials [1].

Unfortunately, concerns about hesitancy to vaccinate against COVID-19 are already emerging [2]. Some of the hesitancy arises understandably from concerns that "shortcuts", especially related to safety, might be undertaken as the typically decade(s)-long vaccine development timeline may be compressed to 12–18 months or less [3]. Another factor may be the perception by the general public of greater risk with new "exotic" technologies [4]. The poor public acceptance of genetically modified foods should be a cautionary tale [5]. Clearly, whatever can be done to increase the scientific literacy of various stakeholders by transparently communicating available information on the benefits and risks of the platform technologies used by COVID-19 and other new vaccines may help.

Accordingly, in this and several adjacent issues, Vaccine is publishing several Brighton Collaboration Standardized Templates for Collection of Key Information from the Benefit-Risk Assessment of VAccines by TechnOlogy (BRAVATO; formerly the Viral Vector Vaccines Safety or V3SWG) Working Group; they include templates for the following vaccine platform technologies: nucleic acid (DNA and RNA) [6], protein [7], viral vector vaccines (Version 3.0) [8], inactivated viral [9], and live-attenuated viral vaccines [10].

The Brighton Collaboration was launched in 2000 to improve the science of vaccine safety, focusing initially on developing standardized case definitions for adverse events following immunizations (AEFI) [11]. In 2008, in response to the unexpected halting of the "STEP" HIV vaccine efficacy trial using a recombinant adenovirus 5 vector candidate due to a higher rate of HIV acquisition among the vaccine vs. placebo recipients [12], the Brighton Collaboration launched the Viral Vector Vaccines Safety Working Group (V3SWG) [13], with two sets of major activities:

(1) Developing harmonized guidelines for assessing/addressing potential safety issues of concern for viral vector vaccines (see Table 1 [14]) (most were initially identified in the meeting report from a World Health Organization (WHO) Informal Consultation on Characterization and Quality Aspect of Vaccines Based on Live Viral Vectors, WHO HQ, Geneva, 4–5 December 2003) [14]. Topics of guidance published to date include: (a) Adventitious agents and live viral vectored vaccines: Considerations for archiving samples of biological materials for retrospective analysis [15]; (b) Potential for and theoretical consequences of recombination with wild type virus strains [16]; and (c) Defining the interval for monitoring potential adverse events following immunization (AEFIs) after receipt of live viral vectored vaccines [17].
(2) Completing standardized templates with key considerations for a benefit-risk assessment on new vaccine candidates. The V3SWG initially adapted a template for viral vectored vaccines developed by the International AIDS Vaccine Initiative (IAVI) [13]. In addition to updating the viral vector vaccine template (to version 3.0) [8] to better meet the needs for

DOI of original article: https://doi.org/10.1016/j.vaccine.2020.08.009https://doi.org/10.1016/j.vaccine.2020.06.017https://doi.org/10.1016/j.vaccine.2020.06.044https://doi.org/10.1016/j.vaccine.2020.07.028https://doi.org/10.1016/j.vaccine.2020.09.042

https://doi.org/10.1016/j.vaccine.2020.10.072

the COVID-19 vaccines, the V3SWG has since a) taken on the task of developing templates for the full range of vaccine platforms described above (including nucleic acid (RNA and DNA) vaccines [6], protein vaccines [7], inactivated viral vaccines [9], live-attenuated viral vaccines [10], and (b) renamed itself the Benefit-Risk Assessment of VAccines by TechnolOgy (BRAVATO) Working Group given its now broader remit. These templates provide a detailed and standardized description of the platform or vaccine and highlight safety considerations for each platform or vaccine, culminating in a summarized risk assessment. The templates aim to increase the comparability and transparency of information, provide a checklist-like tool for managing potential complex risks, and facilitate effective scientific discussion among stakeholders.

In the templates, BRAVATO intends to focus on the key questions related to the essential safety and benefit-risk issues relevant for the intrinsic properties of the vaccine components. There are many other aspects of quality, manufacturing, and implementation that can play an important role in vaccine safety, but BRAVATO has chosen to keep some of those issues out of templates' scope, in order to summarize information that is most useful for a majority of the stakeholders.

The BRAVATO (V3SWG) viral vaccine vector template was the first of the templates to be developed; the subsequent versions of which now collect information on the characteristics of (1) the wild type virus from which the vector is derived; (2) the viral vector itself before incorporation of the foreign antigen; and (3) the final recombinant viral vector vaccine to be administered in animals and humans, toxicity and immunogenicity, with an assessment of overall adverse effects and risk. It is a living document, and experience accumulated during completion of the first version of the viral vector vaccine template, and during development of templates for other vaccine platforms, has resulted in modifications to the initial template which optimize its utility.

The first version (version 1.0) of the BRAVATO (V3SWG) viral vector template was published in 2015 with a description of the yellow fever 17D vaccine vector [19,19], which has been used for construction of recombinant vaccines for Japanese encephalitis [20] and Dengue fever [21]. This same version of the template was also used to describe a vesicular stomatitis virus (VSV) based vector [22] and a VSV-based Ebola vaccine, rVSVΔG-ZEBOV-GP [23], which was used successfully in a ring vaccination trial in Guinea [24]. Presentation of this completed BRAVATO (V3SWG) Ebola vaccine template to the WHO Global Advisory Committee on Vaccine Safety (GACVS) on June 5–6, 2019 resulted in GACVS endorsing the template for use in review of other Ebola vaccines "as it offers a structured approach to evaluating safety." [25] Accordingly, completed templates describing adenovirus 26 [26] and Modified Vaccinia Ankara (MVA) vector [27] Ebola vaccines, using a second version of the template (v2.0), were discussed at the December 4–5, 2019 GAVCS meeting with similar endorsement for future use [28]. After presentation of the new templates relevant to COVID-19 vaccines at its May 27–28, 2020 meeting, the GACVS recommended that any review of the safety of new vaccines be based on the appropriate Brighton Collaboration standardized templates for benefit–risk assessment of vaccines (by technology platforms) when available and approved, which offer a structured approach to evaluating safety. GACVS advised that templates be pilot-tested in a number of scenarios and then adapted accordingly" [29].

While we anticipate that accumulating experience may result in future modifications, we feel it appropriate in light of the urgency imposed by the COVID-19 pandemic, to make public the latest version of the templates. A detailed history of the development of the vector template, the most recent templates for the vaccine platforms, the publications by the vaccine developers utilizing the templates, and some details of the endorsements from normative bodies are available on https://brightoncollaboration.us/bravato/. The templates are currently being utilized by the Coalition for Epidemic Preparedness Innovations (CEPI)-funded vaccine developers. Other vaccine developers are invited to use them, especially those with vaccine candidates likely to be used in humans in the near future, and therefore have stakeholders who would benefit from clear communications of the benefit-risk information in the templates. Collaboration with BRAVATO (please contact bc-coordinator@taskforce.org) to complete the relevant template, peer review, and potential eventual publication in Vaccine is optional but welcome. To promote transparency, the completed template will be posted and maintained on the Brighton Collaboration website for use/reference by various stakeholders. Furthermore, recognizing the rapid pace of new scientific developments in this domain, suggestions for updates to these completed templates can be submitted for review by BRAVATO. Updating of templates for high priority vaccines like COVID-19 may require encouragement by National Regulatory Authorities and/or National Immunization Technical Advisory Groups. Finally, the Brighton Collaboration welcomes feedback from vaccine developers and other key stakeholders which, after review, may be incorporated into future updates of the templates.

Disclaimer

The findings, opinions, conclusions, and assertions contained in this document are those of the individual co-authors. They do not necessarily represent the official positions of any participant's organization (e.g., government, university, or corporations) and should not be construed to represent any Agency determination or policy.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

We thank 1) Jeroen Kortekaas and Jean-Louis Excler for their helpful review and 2) Emily Smith for preparation of this document. We acknowledge the financial support provided by the Coalition for Epidemic Preparedness Innovations (CEPI) for our work under a service order entitled **S**afety **P**latform for **E**mergency v**AC**cines (SPEAC) Project with the Brighton Collaboration, a program of the Task Force for Global Health, Decatur, GA.

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