**COVID Vaccine Advisory Workgroup**
**Safety & Efficacy Subgroup**
**Meeting Minutes**

**Report Submitted by:** Joshua Crawford, Costi Sifri (co-chairs)
**Date of Meeting:** November 2, 2020

**Members:**

| Name | Organization Name(s) | Email |
|---|---|---|
| Crawford, Joshua | Bon Secours | joshua_crawford@bshsi.org |
| Sifri, Costi | UVA Health, UVA School of Medicine | cds9n@hscmail.mcc.virginia.edu |
| Bachireddy, Chethan | VA Department of Medical Assistance Services (DMAS) | chethan.bachireddy@dmas.virginia.gov |
| Hare, Keith | Virginia Health Care Association/Virginia Center for Assisted Living | keith.hare@vhca.org |
| Andy Le | VA Department of Corrections (DOC) | andy.le@vadoc.virginia.gov |
| Royster, Mike | Institute for Public Health Innovation | mroyster@institutephi.org |
| Schriver, Jordan | Commonwealth Academy Private School | jschriver@ca-empowers.org |
| Stiltner, Rodney | VCU Health Systems (VCUHS) | rodney.stiltner@vcuhealth.org |
| Uzel, Jeannine | VDH CHS Nursing | jeannine.uzel@vdh.virginia.gov |
| Varghese, Reuben | Arlington Health District | rvarghese@arlingtonva.us |
| Williams, Cindy | Riverside | Cynthia.Williams2@rivhs.com |

**Discussions:**

- Review of vaccine safety and efficacy meetings, VRBPAC (10/22/2020) and ACIP (10/30/2020).
- Development and use of a Grading System for systematic analysis of medical and scientific literature for vaccine approval.

**Appendix:**

I. SUMMARY OF VRBPAC MEETING (October 22, 2020)
II. SUMMARY of ACIP Meeting (October 30, 2020)
III. Proposed Grading Criteria

## I. Vaccines and Related Biological Products Advisory Committee (VRBPAC) Web-Conference Date: October 22, 2020

Presentations by:

1. Intro
    - Marion F. Gruber, Ph.D.; FDA VRBPAC Liaison
2. Epi, Virology, Clinical Features
    - Cliff McDonald, M.D.; CDC
3. NIH activities in vaccine development
    - Hilary Marston, M.D.; M.P.H., NIH
4. BARTA activities
    - Robert Johnson, Ph.D.; BARTA
5. CDC plans for vaccine safety and monitoring post-EUA and post-licensure
    - Tom Shimabukuro, M.D., M.P.H., M.B.A.; CDC
6. CDC plans for vaccine efficacy and monitoring post-EUA and post-licensure
    - Stephanie Schrag, D.Phil.; CDC
7. Operational challenges
    - CAPT Janell Routh, M.D., M.H.S.; CDC
8. Vaccine confidence
    - Susan Winckler, R.Ph., Esq.; Reagan-Udall Foundation (RUF)
9. Vaccine chemistry and manufacturing
    - Jerry Weir, Ph.D.; FDA
10. Clinical considerations
    - Doran Fink, M.D., Ph.D.; CBER, FDA
11. Public comments

Some Highlights

- Four candidate vaccines selected by Operation Warp Speed now are in phase 3 efficacy trials
    - Reviews of products, endpoints, discussion from manufacturers
- OWS (NIH) Overview
    - Harmonized protocols for safety and efficacy, use collaborating clinical trial networks, through the COVID-19 Prevention Network (CoVPN, composed of 4 separate NIH and DOD vaccine clinical trial networks), collaborating labs for secondary endpoints (immune responses – infection vs vaccination responses, neutralization anti-S IgG assays, T-cell responses), unified DSMB, unified statistical analysis plan
    - Primary endpoint = prevention of COVID-19 disease (PCR confirmed)
- Safety
    - Solicited local/systemic AEs through 7d, unsolicited AEs through 28d, medical AE/severe AEs up to 2y (DSMB reviewed)
- Efficacy

    - FDA set >50% threshold, harmonized efficacy for Operation Warp Speed >60%, lower bound >30%; subgroup analysis for 65+ years
    - Vaccinology approach (subunit versus whole killed virus)
- EUA vs licensure discussion
    - Risks, benefits, and alternatives to an EUVA
- Unblinding after EUA?
- Concerns for vaccination in underrepresented communities if vaccine trials don't achieve proportionate representation and/or are not sufficiently powered to address underrepresented populations
- Concerns for vaccination in elderly populations (65+ years)
- Concerns for pediatric vaccination (inclusion – yes or no, risk for immune enhancement)
- Discussion around safety monitoring
    - Duration before EUA
    - Duration/blinding after EUA
- Discussion of public impressions
    - RUF queried (a) underrepresented communities and (b) healthcare workers
        - Public mistrust issues identified through initial listening sessions: "Another Tuskegee experiment", "we are the guinea pigs for the rich", "I don't want to keep getting used", "the more they study me the more they know how to get rid of me"
        - Other issues identified by listening sessions: people are interested in the science, they want to know how it relates to them, they want to understand the process, personal relationships matter

YouTube Meeting (8:50)
Briefing Document Hyperlink
Roster Hyperlink

## II. ACIP Presentation. October 30, 2020

Agenda Hyperlink
Meeting Hyperlink

## III. Proposed Research Grading Criteria

We propose to use the following grading criteria to assess the quality of evidence of COVID-19 vaccine studies, reports, and announcements. The Vaccine Safety and Efficacy Subgroup expects that safety and efficacy studies used to determine Emergency Use Authorization (EUA) or licensure for a COVID-19 vaccine will primarily be based on studies with a Grade 1 or Grade 2 strength of evidence. Studies with a Grade 4 strength of evidence will be considered to be poor and are not anticipated to be of sufficient strength to support endorsement of vaccination recommendations by the Subgroup.

We propose to collate a bibliography of key studies and reports, including summary information and Grading strength, to help inform the Working Group.

Table. Grading Criteria.

| Study Type | Strength of Evidence (low=4, medium=3, high=2, very high=1) | |
|---|---|---|
| | Safety (S) | Efficacy (E) |
| Phase 3 Randomized Controlled Trials, Peer-reviewed Studies | $1^S$ | $1^E$ |
| Phase 4 Trials, Peer-reviewed Studies (e.g. post-EUA, post-licensure) | $1^S$ | $1^E$ |
| Phase 3 Randomized Controlled Trials, Preprint Studies (e.g. MedRxiv) | $2^S$ | $2^E$ |
| Phase 4 Trials, Preprint Studies (e.g. post-EUA, post-licensure) | $2^S$ | $2^E$ |
| Phase 1/Phase 2 Studies | $2^S$ | n/a |
| Cohort or Case Control Studies | $3^S$ | $3^E$ |
| Preclinical Studies | $3^S$ | n/a |
| Commercial Reports (white papers, press announcements) | $4^S$ | $4^E$ |
| Case Reports | $4^S$ | n/a |