

MEMORANDUM DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
Center for Biologics Evaluation and Research
Office of Vaccines Research and Review
(b) (6)

Date: December 22, 2020

From: (b) (6)

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Sponsor: Moderna Therapeutics

Subject: Review of Preclinical Studies and Clinical Diagnostic Assays for
mRNA-1273 COVID-19 Vaccine

Recommendation

The totality of the data reviewed in this submission support the use of mRNA-1273 vaccine under EUA.

Pre-Clinical Studies for mRNA-1273

Preclinical studies were done in mice (BALB/c, C57BL/6, C3H x C57BL/6), rats, hamsters, and non-human primates (NHPs). These studies were done either by the VRC/DMID/NIAID under IND 19635 or by Moderna under IND 19745.

First, we will present data on protection in the models tested (mice, hamsters, non-human primates (NHP)), as this is perhaps the more important issue. Second, we will present the immune responses in these animals, both humoral and cellular.

Studies in mice

These study were conducted by the VRC/DMID/NIAID or by Moderna.

Protection to challenge

Adult BALB/c mice were vaccinated with 0.01 µg, 0.1 µg, or 1 µg of mRNA-1273 at weeks 0 and 3 (Study VRC01). Mice were challenged by intranasal (IN) inoculation with a mouse-adapted (MA) SARS-CoV-2 (at 10⁵ PFU, a lethal challenge dose) at week 8. The MA SARS-CoV-2 has two amino acid changes in the ACE2 receptor-binding

domain (RBD). Disease was assessed by weight loss, viral load in lungs, viral load in nasal turbinates, and lung hemorrhage. Immune responses were evaluated. While there was no evidence of disease in the vaccinated groups, there was a dose-dependent effect on viral loads. A dose of 1 µg protected against virus replication in the lungs and nasal turbinates, while a dose of 0.1 µg reduced the viral load in the lungs by 2 logs and 0.01 µg reduced it by 0.5 logs. In another study, mice immunized with mRNA-1273 intramuscularly (IM) at 1 µg and 0.1 µg and boosted at 4 weeks were challenged IN 3 weeks post boost (week 7). Two weeks after challenge, data showed that the groups inoculated with 1 or 0.1 µg doses were protected from virus replication in the lungs, and the 1 µg group was protected from virus replication in the nose. In a study to evaluate whether a single dose was effective, mice were inoculated with 10 µg or 1 µg and challenged 7 weeks later. Interestingly, mice in both groups were protected from virus replication in the lungs, although there was no evidence of serum-neutralizing antibodies, raising the possibility that other mechanism may be operating.

A second study (VRC02) was carried out in aged mice. BALB/c mice more than one-year old were immunized with 0.1 µg or 1 µg of mRNA-1273 at week 0 and boosted at week 3 with the same doses. In addition, mice were inoculated with double-inactivated (DIV) SARS-CoV-2 and a PBS control. [The inactivation was by both formalin and ultraviolet light.] The dose of DIV was chosen that had been shown to be immunogenic, and its evaluation here was because inactivated vaccines against other viruses have been shown to induce enhanced respiratory disease (ERD) when subsequently exposed to the infectious virus and thus would act as a control for the induction of ERD. ERD has been shown to result from an immune response with a Th2 bias, and thus it was important to show that mRNA-1273 induced a stronger Th1 response relative to a Th2 response. This response was evaluated and mRNA-1273 showed a stronger Th1-type response, compared with the DIV response. Four weeks after the boost, mice were challenged with the MA SARS-CoV-2, and mice were followed for weight loss over the next 4 days. At days 2 and 4, mice were assessed for virus replication in the lungs and nasal turbinates, and lungs were evaluated for the presence of hemorrhage. Weight loss was reduced in the mRNA-1273-vaccinated groups, with 1 µg dose more effective than the 0.1 µg dose. Significant weight loss was found in the PBS control group, and the weight loss in the DIV group was similar to the PBS control group. Viral loads in the lungs and nasal turbinates were lower in both mRNA-1273 groups with the 1 µg dose having lower amounts of virus than the 0.1 µg dose. The DIV group did not protect from infection, as indicated by the similar levels of viral RNA with the PBS control. Lung hemorrhage was not apparent until day 4, and the 1 µg dose was superior to the 0.1 µg dose.

Immunogenicity in mice

Three strains, BALB/c, C57BL/6, and C3H x C57BL/6, were used in 3 studies to assess immunogenicity of SARS-CoV-2 S vaccines (VRC01; IND 19635).

First study: A vaccine lot that was representative of Moderna's mRNA-1273 vaccine was inoculated into 6-week-old female BALB/c, C57BL/6, and C3H x C57BL/6 mice (100 mice total). Mice received 2 doses IM of 0.01 µg, 0.1 µg or 1 µg of mRNA-1273 in

the right hind leg in a volume of 50 µL at week 0 and week 3. Immunogenicity readouts were done at week 2 and week 5 using an IgG ELISA (SARS-CoV-2 S-2P spike) and a pseudovirus neutralization assay. Two weeks post-boost, sera were collected and tested by ELISA to assess binding IgG antibody to SARS-CoV-2 S-2P. Two-way ANOVA was used to compare post-prime and post-boost. At the 1 µg dose level, significantly higher binding IgG antibody titers were observed post-boost in BALB/c and C57BL6 mice immunized with 1 µg of mRNA-1273. Mice immunized with 1 µg dose had significantly higher neutralizing antibody responses than those in the 0.1 µg group ($p < 0.0001$). Neutralizing antibody responses were undetectable in mice immunized with 0.01 µg mRNA-1273.

Second study: Six-week-old female BALB/c mice ($n=30$) received a single dose of 0.1 µg, 1.0 µg or 10 µg of mRNA-1273 in an intramuscular injection in the right hind leg in a volume of 50 µL. Immunogenicity was assessed by measurement of binding IgG antibodies to SARS-CoV-2 prefusion stabilized spike protein (S-2P) and by a lentiviral pseudovirus neutralization assay. S-binding antibodies were induced in mice immunized with one dose of 1 or 10 µg of mRNA-1273, with the 10 µg dose eliciting neutralizing antibody activity that increased between week 2 and week 4.

Third study: Comparison of immunogenicity in BALB/c and C3H x C57BL/6 mice ($n=60$) of SARS-CoV-2 S-2P mRNA with wild-type SARS-CoV-2 S mRNA and a SARS-CoV-2 S mRNA construct containing mutations in the furin-cleavage site (S-2P RARR or S-2P_RARR_GSGG). The immunogenicity of mRNA-1273 (S-2P_RARR) was compared with that of a wild-type SARS-CoV-2 spike (S) mRNA construct (without the 2-proline mutation) and a SARS-CoV-2 mRNA encoding an S protein containing mutations in the furin cleavage site (S-2P_RARR_GSGG). Mice immunized with 1 µg of each of the SARS-CoV-2 S mRNA constructs had significantly higher neutralizing antibody responses than mice immunized with 0.1 µg. Serum from mice immunized with the 0.1 µg dose of any of the constructs did not have detectable neutralizing activity. Stabilized SARS-CoV-2 S with the 2P mutation induced more potent IC50 neutralizing activity than did the WT S. Inclusion of the native S1/S2 furin cleavage site or replacing the furin cleavage site with a GS linker to produce a single-chain construct did not have significant effect on immunogenicity.

The data from these studies demonstrated that mRNA expressing SARS-CoV-2 S-2P is a potent immunogen, that neutralizing activity can be elicited with a single dose, and that binding-antibody responses are proportionate to neutralizing antibody responses in mice.

Moderna also undertook studies in mice to determine the immunogenicity of mRNA-1273 and address the risk of enhanced respiratory disease (ERD) through antibody dependent enhancement. Studies MOD-3937, MOD-3938, MOD-3940 (IND 19745) evaluated the immunogenicity of mRNA-1273 DP and addressed the theoretical concern of ERD in young, female BALB/c mice in comparison with SARS-CoV-2 S-2P protein (the spike protein with the two proline pre-fusion stabilizing mutations) adjuvanted with aluminum hydroxide (alum; (b) (4)). Groups of BALB/c mice were

vaccinated with 1 µg (n = 7) or 10 µg (n = 8) of mRNA-1273 DP, 10 µg of SARS-CoV-2 S-2P protein + 250 µg of (b) (4) (n = 8), or PBS (n = 3). Vaccine or control was administered via IM injection into the hind leg at week 0, and animals received a boost at week 2. At Week 4 (Day 28), serum was collected from all animals and assessed for IgG antibody binding to SARS-CoV-2 S protein by ELISA and for neutralizing antibody activity against homologous SARS-CoV-2 S protein via a pseudotyped lentivirus reporter neutralization assay. Spike-specific IgG2a and IgG1 antibody titers were also measured by ELISA, and subclass ratios were calculated, as the ratio of IgG antibody subclasses is considered a surrogate measurement to indicate the Th1/Th2 response. For example, a Th2-directed CD4 T-cell response is characterized by the presence of IgG1 antibody subclass titers and a corresponding lack of IgG2a antibody subclass titers, while the presence of IgG2A corresponds to a Th1 response. One day after serum collection (Day 29), the 10 µg SARS-CoV-2 S-2P protein + 250 µg (b) (4) group animals were restimulated with 10 µg of SARS-CoV-2 S-2P protein (without adjuvant). Mice in the mRNA-1273 groups (1 µg and 10 µg) were not restimulated. Four days after restimulation (Day 33), spleens were collected, and splenocytes isolated from each group of mice were stimulated for 24 hours in vitro to activate antigen-specific splenocytes using two S-peptide pools that in combination cover the entire SARS-CoV-2 spike protein. After the 24-hour stimulation with the 2 S peptide pools, culture supernatant was collected to measure the levels of secreted cytokines using (b) (4) analysis.

Binding and neutralizing antibody titers were measured, as high levels of binding antibody with low levels of neutralization activity have been associated with disease enhancement mediated by immune complex deposition and complement activation. The results demonstrated that mRNA-1273 elicited a high IgG2a/IgG1 antibody ratio, while , mice administered 10 µg of SARS-CoV-2 S-2P protein + 250 µg of (b) (4) had high titers of IgG1 and low titers of IgG2a antibodies. In addition, in vitro stimulation with the 2 S peptide pools, the splenocytes from mRNA-1273-immunized mice secreted more IFN-γ than IL-4, IL-5, or IL-13, indicating a Th1-directed immune response, whereas, 10 µg of SARS-CoV-2 S-2P protein + 250 µg of (b) (4) induced a Th2-directed response.

Reviewers' comments

These results demonstrate that, unlike the SARS-CoV-2 S-2P protein adjuvanted with alum, which elicits a Th2-directed response, mRNA-1273 drives a Th1-directed immune response and induces robust binding and neutralization activity, an immune signature not predicted to drive vaccine-associated ERD.

Considering the studies from both the VRC and Moderna, the results were important for several reasons. Because certain vaccines (such as inactivated virus vaccines for RSV and measles) have caused ERD, it has been important to evaluate the potential for whether vaccines against SARS-CoV-2 could induce ERD, particularly since such a phenomenon was previously reported in pre-clinical studies of vaccines against other coronaviruses, SARS-CoV and MERS-CoV. The studies to assess

whether the mRNA-1273 vaccine could result in ERD were done in animal models. Signs of ERD include increased illness compared with unvaccinated animals, higher virus titers in lungs, and lung pathology showing eosinophilia, mucus production, or neutrophilic alveolitis. In addition, higher binding antibody titers compared with neutralizing antibody titers have been associated with ERD. However, the use of sub-optimal doses of the vaccine to allow some virus infection, which might be expected to favor ERD, has not resulted in enhanced disease.

Finally, the results in mice demonstrated that mRNA-1273 protects both adult and aged mice from challenge with a mouse-adapted SARS-CoV-2. In addition, the vaccine elicited a Th1-biased immune response, and sub-optimal doses of vaccine did not result in enhanced disease.

Studies in NHPs

Protection against challenge and immunogenicity studies

These NHP studies were described in IND 19635 amendments 20, 21, 22, and 31. Two studies in rhesus macaques, VRC04 and VRC07, were done by the VRC. One of the studies was performed to assess immunogenicity (see below) and the other to evaluate protection against SARS-CoV-2 challenge. To determine if mRNA-1273 protects NHPs from disease after challenge, adult rhesus macaques (four females and four males 3 – 6 years old) were immunized IM with 10 or 100 µg of mRNA-1273 on week 0 and week 4. At week 8 (4 weeks after the second vaccination), monkeys were challenged with a total of 7.6×10^5 PFU of SARS-CoV-2. Viral inoculum was administered as 5.7×10^5 PFU in 3 mL via intratracheal route (IT) and 1.9×10^5 PFU in 1 mL via intranasal route (IN) (0.5 mL into each nostril). Serum was collected pre-immunization, bi-weekly post-prime and post-boost, and at days 7 and 14 post-challenge. Viral infection was determined by measuring the presence of SARS-CoV-2 in nasal swabs and bronchoalveolar lavages (BAL), which were collected post-challenge on days 1, 2, 4, and 7 and 2, 4 and 7, respectively. Lung pathology was assessed on days 7 and 8 post-challenge. Polymerase chain reaction (PCR) was used to quantify viral RNA and subgenomic RNA, the latter was used to quantify replicating RNA in the BAL fluid and nasal swab specimens.

Results demonstrated that mRNA-1273 rapidly limits SARS-CoV-2 replication in upper and lower airways, with significant clearance of virus by day 2 post-challenge compared with PBS-immunized NHPs. There was no detectable viral replication in the BAL from mRNA-1273-immunized NHPs by day 2 following challenge in 7 out of 8 NHPs in both the 10-µg and 100-µg groups. There was no detectable viral replication in nasal swabs of any of the 8 NHPs immunized with 100 µg mRNA-1273 by day 2 post-challenge.

The humoral immune responses assessed were binding IgG and neutralizing antibodies. Binding antibodies were quantified by ELISA, and neutralizing antibodies were quantified by a lentivirus pseudovirus neutralization assay with a (b) (4) readout and confirmed using a live virus neutralization assay. In addition, antibodies that bound to the receptor-binding domain were quantified and assessed for whether these antibodies were able to block the interaction of the virus with its receptor ACE2.

Binding antibodies were induced after the first dose and boosted after the second dose, with the response greater in the 100-µg group than in the 10-µg group. There were corresponding increases in the activity of neutralizing antibodies (assessed by both assays), and ACE2-blocking antibodies also increased. Cellular immune responses were evaluated, and these indicated a Th1 bias.

Reviewers' Comments

mRNA-1273 induces both IgG binding antibodies and neutralizing antibodies, and monkeys are protected from SARS-CoV-2 challenge. Importantly, mRNA-1273 immunization of NHPs does not lead to enhanced lung inflammation or detectable virus post-challenge and did not induce inflammatory lung cytokine/chemokine responses in the BAL.

Studies in Hamsters

Recent research has indicated that the hamster is a relevant model for SARS-CoV-2 pathogenesis. Moderna contracted the University of Texas Medical Branch, Galveston, to perform this test (study number UTMB01).

Female Syrian hamsters 6 to 7 weeks old (15/group) were administered 1 µg, 5 µg, or 25 µg of mRNA-1273 on a prime (week 0, Day 1) and boost (week 3, Day 22) schedule or a 25 µg of mRNA-1273 or PBS as a prime only. An equal volume of vaccine was administered IM into each hind leg (50 µL per dose). Sera were collected on Day 21 and on Day 42 (week 6). Sera were tested for SARS-CoV-2 S-specific IgG and RBD-specific IgG by ELISAs, and also evaluated for their neutralizing activity by a plaque-reduction neutralization test (PRNT), a live virus assay.

All animals were challenged on Day 43 with wild-type SARS-CoV-2 (USA-WA/2020) at 10⁵ plaque-forming units (PFU) by the intra-nasal route. Body weights were measured through Day 14 post challenge, and serum samples were collected on Days 2, 4 and 14 post challenge to assess the antibody titers to S and NP by ELISA as well as neutralizing activity by PRNT. Some hamsters were sacrificed on Days 2, 4 and 14 to evaluate viral load by plaque assay and actively replicating virus by subgenomic RT-qPCR. Lung pathology was also assessed at these time points.

Immunization with mRNA-1273 elicited S- and RBD-specific IgG titers in all groups and neutralizing titers in the prime/boost groups and a subset of the animals in the single-dose group. All binding antibodies were increased following the boost. Complete neutralizing seroconversion in all animals was only achieved in the prime/boost groups, where neutralizing titers with the 1, 5, and 25 µg doses met or exceeded the highest titers found with convalescent serum.

After challenge, minimal weight loss was found in the vaccinated animals receiving the prime/boost regimen with all dose levels except for one hamster in the 5-µg group. Also, one hamster in the single-dose group experienced weight loss, while the others did not. By Day 14 post challenge, binding antibodies to S and neutralizing antibodies increased

(except for the 1-µg dose group). Antibodies to NP were detected after challenge, although the titers in the vaccinated animals were lower than in the control group. Evaluation of viral loads by measuring virus via plaque assay and by RT-qPCR in the nasal turbinates and lungs showed that viral loads were below the limit of detection at Day 4 post challenge of the groups with the prime/boost regimen by plaque assay, and virus replication by RT-qPCR in the lung was not detected with the 5 and 25 µg doses and only detected in one animal with the 1 µg dose. Assessing virus replication in the nasal turbinates showed that animals were partially protected. Lung histopathology over the 14-day monitoring showed that there was only moderate inflammation.

Reviewers' Comments

These hamster studies indicated that the vaccine provided protection from disease but does not provide sterilizing immunity.

Biodistribution Studies

Biodistribution studies were not performed on the mRNA-1273 vaccine, but on vaccines manufactured using the same LNP platform, as it is recognized that it is the LNP component rather than the mRNA that determines the cell entry and tissue distribution. The results of studies in female Sprague-Dawley rats from Moderna and other investigators have shown that the tissue distribution depends on the route of administration, but whatever the route, the vaccine does not persist more than 7 days after inoculation (Study 5002121). Moderna have used their biodistribution and persistence studies with other mRNA vaccines manufactured using the same LNP formulation as evidence that biodistribution and persistence do not represent safety concerns.

Reviewers' Comments

The reader is referred to a paper by the (b) (4) groups, who followed the fate of a (b) (4) mRNA LNP administered to mice by six different routes (IV, IP, IM, IT, SC, ID) using whole mouse imaging (b) (4). This result has implications for safety in that the ability of the mRNA-LNP vaccine to migrate to distal sites including the fetus in pregnant females is not indicated by the data. Because of the kinetics of decay, the quantity of mRNA inoculated, and the lability of RNA in vivo once dissociated from the LNP, this possibility is remote. Furthermore, it has been posited that mRNA could become reverse transcribed by cellular reverse transcriptases into double-stranded DNA and integrate into host DNA, specifically fetal DNA. Without addressing the implausibility of the last part except to point out that in this scenario reverse transcription might also occur with host mRNA, which would be in greater abundance, traversing into the fetus would be improbable at best.

We conclude that biodistribution and persistence of mRNA-1273 is not a significant risk to vaccine recipients of mRNA vaccines.

Clinical Diagnostic Assays

These assays were done to ascertain whether participants in the clinical trials were or had been exposed to SARS-CoV-2. They were also used to confirm COVID-19 cases for evaluation of Phase 3 study efficacy endpoints.

Roche Elecsys ELISA was used for the detection of SARS-CoV-2 nucleocapsid (or N) protein. This assay received EUA from the FDA in May 2020, and a letter confirming the granting of the EUA is included.

Two diagnostic assays were used for the assessment of the Phase 3 clinical study efficacy endpoints. The Roche Elecsys Anti-SARS-CoV-2 assay was used for the evaluation of SARS-CoV-2 serostatus of study participants before vaccination. The Viracor Eurofins Clinical Diagnostics RT-qPCR was used to determine the virus infection status of study participants before vaccination and to confirm COVID-19 cases for the evaluation of clinical-study endpoints.

RT-qPCR for the detection of SARS-CoV-2 RNA

This RT-qPCR assay is a quantitative diagnostic test for SARS-CoV-2 from Viracor Eurofins Clinical Diagnostics, which has been granted an EUA. The assay is performed in a CAP-accredited and CLIA-certified laboratory under contract. The assay is used to detect SARS-CoV-2 viral ribonucleic acid (RNA) in nasopharyngeal swab, nasal swab, nasopharyngeal wash, nasal wash, oropharyngeal swab and bronchoalveolar lavage. The assay is used to screen participants for exposure to SARS-CoV-2 prior to enrolling in the trial as well as to confirm COVID-19 cases. The PCR assay is designed to detect the SARS-CoV-2 N gene and is a laboratory test developed by Viracor Eurofins Clinical Diagnostics. The assay uses TaqMan chemistry (primers and probe) and is read on an ABI 7500 SDS Instrument.

Validation of the RT-qPCR assay by Viracor for the quantification of SARS-CoV-2 RNA

This RT-qPCR assay for the quantification of SARS-CoV-2 RNA received an EUA from FDA.

The submitted validation report includes the extraction and RT-qPCR method along with assessment of analytical sensitivity via limit of detection (LOD) and lower limit of quantification (LLOQ), linearity and dynamic range, accuracy, intra-assay and inter-assay precision (reproducibility) and stability and acceptance criteria for each of these approaches, for the SARS-CoV-2 RT-qPCR assay.

Moderna has included validation reports for the following protocols:

- 21120.8918 SARS-CoV-2 (COVID-19) RT-qPCR Validation Report. This validation report includes the extraction method, assessment of limit of detection (LOD), linearity and dynamic range, clinical evaluation, intra-assay and inter-assay precision (reproducibility), inclusivity, and cross-reactivity, and acceptance criteria for each of these approaches. This validation plan was primarily composed using guidelines recommended by the US FDA (see: Policy for

Diagnostics Testing in Laboratories Certified to Perform High Complexity Testing under CLIA prior to Emergency Use Authorization for Coronavirus Disease-2019 during the Public Health Emergency - Immediately in Effect Guidance for Clinical Laboratories and Food and Drug Administration Staff, document issued on February 29, 2020). Table 1 is a summary of the performance characteristics with their acceptance criteria, validation results, and pass/fail status.

Table 1. Summary of validation criteria and results for SARS-COV-2 RT-qPCR assay in swab and saliva specimens

Performance Characteristic	Acceptance Criteria	Validation Results	Pass/Fail
(b) (4)			Pass
			Pass
			Pass
			Pass
			Pass
			Pass
			Pass

Validation assessments

Sample preparation

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Nucleic acid extraction

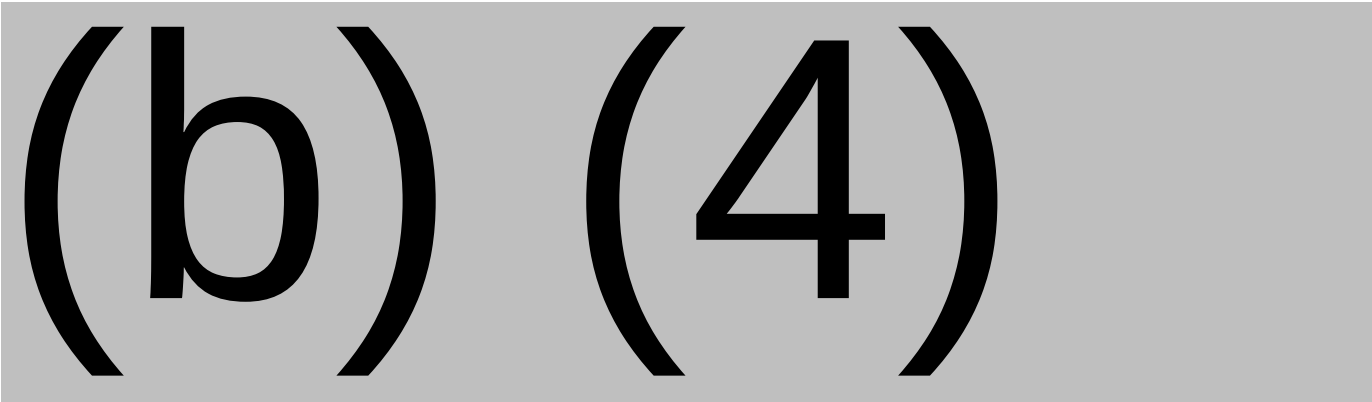
Nucleic acid extraction for upper/lower respiratory samples was performed following instructions in SOP 21120.705 NucliSens easyMAG Total Nucleic Acid Extraction. (b) (4)

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Nucleic acid amplification and detection

Nucleic acid amplification was performed as described in SOP 21120.461 Real-Time PCR and RT-PCR Using ABI 7500 SDS Instruments with the following modifications. –

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Reviewers' comment

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Clinical evaluation

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Reviewers' Comments

The validation report for the RT-qPCR assay by Viracor assay indicates that the assay is appropriate for its intended purpose.

Roche Elecsys ELISA for the detection of SARS-CoV-2 nucleocapsid (or N) protein

This assay received EUA from the FDA in May 2020, and a letter confirming the granting of the EUA was included. The assay is performed on the Roche Cobas 8000 machine at PPD Global Central Labs in Kentucky, a CAP-accredited and CLIA-certified testing laboratory.

The assay is a sandwich format, and the results are determined automatically in about 18 minutes. The first incubation is with 20 µL of sample (serum or plasma), with biotinylated SARS-CoV-2-specific recombinant antigen and SARS-CoV-2-specific recombinant antigen labelled with ruthenium complex to form a sandwich complex. The addition of streptavidin-coated microparticles results in the complex becoming bound to the solid phase *via* the streptavidin/biotin interaction. The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are removed with the ProCell/ProCell M. Application of a voltage to the electrode induces chemiluminescent emission, which is measured by the photomultiplier. Results are determined automatically by the software by comparing the electro chemiluminescence signal of the sample with signal of the cutoff value previously obtained by calibration.

Accuracy, correlation, matrix effects, precision, analytical sensitivity (LLOQ) analytical specificity, linearity and ULOQ, maximum dilution, and stability were assessed and found to be appropriate.

Reviewers' Comments

The validation report for the Roche Elecsys ELISA indicates that the assay is appropriate for its intended purpose.

Reviewers' Conclusions for the Diagnostic Clinical Assays

Both the RT-qPCR assay for the detection of SARS-CoV-2 RNA being carried out by Viracor Eurofins Clinical Diagnostics and the Roche Elecsys Anti-SARS-CoV-2 ELISA being carried out at PPD Laboratories, are appropriate for the assessment of SARS-CoV-2 infection during the clinical trials of the Moderna mRNA-1273 vaccine.

Other Immunogenicity Assays in Development

While the outcome of the clinical trial is to be determined by clinical efficacy disease endpoints, several exploratory immunological assays will be used to establish the immune responses to vaccination with the ultimate goal of identifying immune correlates of protection. At this stage, the assays are in development and have not been qualified. It is expected that for the BLA, the assays will be validated. The ELISA for SARS-CoV-2 S protein is undergoing validation by PPD, and two neutralization assays are being considered, one involving a live virus and another using a pseudovirus assay.

