1.12.14 ENVIRONMENTAL ASSESSMENT: CLAIM FOR CATEGORICAL EXCLUSION

ModernaTX, Inc. claims a categorical exclusion from the requirement to prepare an Environmental Assessment or an Environmental Impact Statement (EIS) based on 21 CFR 25.31(c) that this application for marketing approval of a biologic product for substances that occur naturally in the environment when the action does not alter significantly the concentration or distribution of the substance, its metabolites, or degradation products in the environment.

In accordance with 21 CFR 25.15(a), ModernaTX, Inc hereby confirms that it complies with the categorical exclusion criteria and acknowledges that to the best of its knowledge no extraordinary circumstances exist.

Background information to determine whether mRNA-1273 qualifies for categorical exclusion is included below.

Background Information to justify Categorical Exclusion Claim

ModernaTX, Inc. is developing a novel messenger RNA (mRNA)-based COVID-19 vaccine, mRNA-1273 encodes the full length SARS-COV2 spike protein. The single mRNA Drug Substances are formulated in a mixture of 4 lipids to form a drug-lipid complex (lipid nanoparticle [LNP]). The 4 lipids are heptadecan-9-yl 8-((2hydroxyethyl)(6-oxo6(undecyloxy)hexyl)amino)octanoate (SM-102); cholesterol; 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC); and 1,2-dimyristoyl-sn-glycerol, methoxypolyethyleneglycol (PEG2000-DMG). SM-102 and the 3 commercially available lipids contribute to the overall pharmaceutical properties of the LNPs and are provided as a sterile liquid for injection at a concentrations of 0.2 mg mRNA/mL, respectively, in 20 mM Tromethamine (Tris), 4.3 mM acetate, 87 g/L sucrose. As is described elsewhere, the mRNA component consists of naturally occurring nucleic acids and the ultimate protein sequence for the viral spike protein has not been altered.

The following components are considered naturally derived: cholesterol, DSPC and the mRNA and are therefore excluded from this evaluation.

The proprietary lipids SM-102 and PEG2000-DMG were evaluated in a series of nonclinical toxicology studies (Study no's: 5002045, 9800399, 5002231, 9800399, 5002034, 5002158, 5002033 5002400 9601567 9601568, 2308-245 and 20248897). These evaluations indicated

standard toxicology responses to lipids with no hormonal, reproductive effects or effects on developing offspring.

The estimated annual usage of these lipids in the United States is anticipated to be between (b) (4) (b) (4) year for PEG2000-DMG and (b) (4) year for SM-102. Based upon these estimates the yearly environmental exposure is anticipated to fall well below 1 part per billion.

The requested action therefore qualifies for a categorical exclusion from the requirement to prepare an EA, per 21 CFR § 25.31(b), because the estimated concentration of the substance at the point of entry into the aquatic environment is estimated to be below 1 part per billion. To the applicant's knowledge, no extraordinary circumstances exist that would warrant the preparation of an EA. *(REF MANUAL OF POLICIES AND PROCEDURES CENTER FOR DRUG EVALUATION AND RESEARCH MAPP 5015.7 Rev. 1 Originating Office: Office of Pharmaceutical Quality Effective Date: 03/06/03; 10/10/17)*