spinal cord membranes), herpangina (brief fever accompanied by ulcerated lesions of the throat), and myopericarditis (inflammation of heart tissue).

(b) *Classification.* Class I (general controls). The device is exempt from the premarket notification procedures in subpart E of part 807 of this chapter subject to § 866.9.

[47 FR 50823, Nov. 9, 1982, as amended at 65 FR 2311, Jan. 14, 2000]

### § 866.3165 *Cryptococcus neoformans* serological reagents.

(a) *Identification. Cryptococcus neoformans* serological reagents are devices that consist of antigens used in serological tests to identify antibodies to *Cryptococcus neoformans* in serum. Additionally, some of these reagents consist of antisera conjugated with a fluorescent dye (immunofluorescent reagents) and are used to identify *Cryptococcus neoformans* directly from clinical specimens or from cultured isolates derived from clinical specimens. The identification aids in the diagnosis of cryptococcosis and provides epidemiological information on this type of disease. Cryptococcosis infections are found most often as chronic meningitis (inflammation of brain membranes) and, if not treated, are usually fatal.

(b) *Classification.* Class II (special controls). The device is exempt from the premarket notification procedures in subpart E of part 807 of this chapter subject to § 866.9.

[47 FR 50823, Nov. 9, 1982, as amended at 63 FR 59226, Nov. 3, 1998]

### § 866.3169 Hepatitis C virus antibody tests.

(a) *Identification.* A hepatitis C virus (HCV) antibody test is identified as an in vitro diagnostic device intended for use with human serum, plasma, or other matrices as a prescription device that aids in the diagnosis of HCV infection in persons with signs and symptoms of hepatitis and in persons at risk for hepatitis C infection. The test is not intended for screening blood, plasma, cell, or tissue donors.

(b) *Classification.* Class II (special controls). The special controls for this device are:

(1) The labeling required under § 809.10(b) of this chapter must include:

(i) A prominent statement that the test is not intended for the screening of blood, plasma, and cell or tissue donors.

(ii) Limitations, which must be updated to reflect current clinical practice and disease presentation and management. The limitations must include, but are not limited to, statements that indicate:

(A) When appropriate, the performance characteristics of the test have not been established in populations of immunocompromised or immunosuppressed patients or, other special populations where test performance may be affected.

(B) The detection of HCV antibodies indicates a present or past infection with hepatitis C virus, but does not differentiate between acute, chronic, or resolved infection.

(C) The specimen types for which the device has been cleared, and that use of the test with specimen types other than those specifically cleared for this device may result in inaccurate test results.

(D) Test results are to be interpreted by qualified licensed healthcare professionals in conjunction with the individual's clinical presentation, history, and other laboratory results.

(E) A non-reactive test result may occur early during acute infection, prior to development of a host antibody response to infection, or when analyte levels are below the limit of detection of the test.

(iii) A detailed explanation of the principles of operation and procedures for performing the test.

(2) Design verification and validation must include the following:

(i) A detailed device description, including all parts that make up the device, ancillary reagents required but not provided, an explanation of the device methodology, and design of the antigen(s) and capture antibody(ies) sequences, rationale for the selected epitope(s), degree of amino acid sequence conservation of the target, and the design and nature of all primary, secondary, and subsequent standards used for calibration.

(ii) Documentation and characterization (*e.g.*, supplier, determination of identity, and stability) of all critical reagents (including description of the antigen(s) and capture antibody(ies)), and protocols for maintaining product integrity throughout its labeled shelf life.

(iii) Risk analysis and management strategies, such as Failure Modes Effects Analysis and/or Hazard Analysis and Critical Control Points summaries and their impact on test performance.

(iv) Final release criteria to be used for manufactured test lots with appropriate evidence that lots released at the extremes of the specifications will meet the claimed analytical and clinical performance characteristics as well as the stability claims.

(v) Stability studies for reagents must include documentation of an assessment of real-time stability for multiple reagent lots using the indicated specimen types and must use acceptance criteria that ensure that analytical and clinical performance characteristics are met when stability is assigned based on the extremes of the acceptance range.

(vi) All stability protocols, including acceptance criteria.

(vii) Final release test results for each lot used in clinical studies.

(viii) Multisite reproducibility study that includes the testing of three independent production lots.

(ix) Analytical performance studies and results for determining the limit of blank (LoB), limit of detection (LoD), cutoff, precision (reproducibility) including lot-to-lot and/or instrument-to-instrument precision, interference, cross reactivity, carryover, hook effect, seroconversion panel testing, matrix equivalency, specimen stability, reagent stability, and cross-genotype antibody detection sensitivity, when appropriate.

(x) Analytical sensitivity of the test is the same or better than that of other cleared or approved tests.

(xi) Detailed documentation of clinical performance testing from a multisite clinical study. Performance must be analyzed relative to an FDA cleared or approved HCV antibody test, or a comparator that FDA has determined is appropriate. This study must be conducted using appropriate patient samples, with an acceptable number of HCV positive and negative samples in applicable risk categories. Additional relevant patient groups must be validated as appropriate. The samples may be a combination of fresh and repository samples, sourced from geographically diverse areas. The study designs, including number of samples tested, must be sufficient to meet the following criteria:

(A) Clinical sensitivity of the test must have a lower bound of the 95 percent confidence interval of greater than or equal to 95 percent.

(B) Clinical specificity of the test must have a lower bound of the 95 percent confidence interval of greater than or equal to 96 percent.

(3) For any HCV antibody test intended for Point of Care (PoC) use, the following special controls, in addition to those listed in paragraphs (b)(1) and (2) of this section, apply:

(i) Clinical studies must be conducted at PoC sites.

(ii) Additional labeling must include a brief summary of the instructions for use that are appropriate for use in a PoC environment.

[86 FR 66176, Nov. 22, 2021]

### § 866.3170 Nucleic acid-based hepatitis C virus ribonucleic acid tests.

(a) *Identification.* A nucleic acid-based hepatitis C virus (HCV) ribonucleic acid (RNA) test is identified as an in vitro diagnostic device intended for prescription use as an aid in the diagnosis of HCV infection in specified populations, and/or as an aid in the management of HCV-infected patients including guiding the selection of genotype-specific treatment in individuals with chronic HCV infection. The test is intended for use with human serum or plasma. The test is not intended for use as a donor screening test for the presence of HCV antibodies in blood, blood products, or tissue donors.

(b) *Classification.* Class II (special controls). The special controls for this device are:

(1) For all nucleic acid-based HCV RNA tests, the labeling required under § 809.10(b) of this chapter must include:

(i) A prominent statement that the test is not intended for use as a donor