The C-Heading 1 above has been created and hidden in order to get the document's first heading, below, to be numbered properly. The heading below is intentionally numbered with just the last digit of the CTD section, with the parent CTD section number and title in the header, per the "Guidance for Industry: Granularity Document, Annex to M4 Organization of the CTD."

Do not modify the heading numbering below. As the document is being finalized, this hidden text can be deleted and the heading numbering will remain correct.

2. ADVENTITIOUS AGENTS SAFETY EVALUATION [NAME, DOSAGE FORM, MANUFACTURER]

Information assessing the risk of potential contamination with adventitious agents should be provided in this section.

For nonviral adventitious agents:

Detailed information should be provided on the avoidance and control of nonviral adventitious agents (eg, transmissible spongiform encephalopathy agents, bacteria, mycoplasma, fungi). This information can include, for example, certification and/or testing of raw materials and excipients and control of the production process, as appropriate for the material, process and agent.

Reference ICH guidances Q5A, Q5D, and Q6B.

For viral adventitious agents:

Detailed information from viral safety evaluation studies should be provided in this section.

Viral evaluation studies should demonstrate that the materials used in production are considered safe, and that the approaches used to test, evaluate, and eliminate the potential risks during manufacturing are suitable. The applicant should refer to Q5A, Q5D, and Q6B for further guidance.

Information essential to evaluate the virological safety of materials of animal or human origin (eg, biological fluids, tissue, organ, cell lines) should be provided. (See related information in 3.2.S.2.3, and 3.2.P.4.5). For cell lines, information on the selection, testing, and safety assessment for potential viral contamination of the cells and viral qualification of cell banks should also be provided. (See related information in 3.2.S.2.3).

The selection of virological tests that are conducted during manufacturing (eg, cell substrate, unprocessed bulk, or postviral clearance testing) should be justified. The type of test, sensitivity and specificity of the test, if applicable, and frequency of testing should be included. Test results to confirm, at an appropriate stage of manufacture, that the product is free from viral contamination should be provided. (See related information in 3.2.S.2.4 and 3.2.P.3.4). In accordance with Q5A and Q6B, results for viral testing of unprocessed bulk should be included.

In accordance with Q5A, the rationale and action plan for assessing viral clearance and the results and evaluation of the viral clearance studies should be provided. Data can include those that demonstrate the validity of the scaled-down model compared to the commercial scale process, the adequacy of viral inactivation or removal procedures for manufacturing equipment

and materials, and manufacturing steps that are capable of removing or inactivating viruses. (See related information in 3.2.S.2.5 and 3.2.P.3.5).

Reference ICH guidances Q5A, Q5D, and Q6B.