3. Stage 3: Conduct A Detailed Review Of The Available Relevant Toxicological Data To Identify Conditions To Adapt Standard Information Requirements For Reproductive Toxicity

Before any testing is conducted, a thorough data review should be conducted to determine if any adaptation rules beyond CMR classification are met. Appendix R.7.6-4 identifies the procedure for testing approaches and adaptation for Stage 3. Table 2 summaries these approaches and adaptations, and why the general rules for adaptation are not met indicating the studies must be conducted.

Table 2:Examination of the procedure for testing approaches and adaptation for Stage 3

Testing Approaches And Adaptation	Does the substance meet these criteria?
Stage 3.1.1 – Adaptation based on existing information not carried out according to GLP or the test methods indicated in the test method regulation	No, there is no existing information not carried out according to GLP or the test methods indicated in the test method regulation
Stage 3.1.2 – Adaptation based on existing historical human data	No, no historical human data was identified for reproductive toxicity of the registered substance.
Stage 3.1.3 – Adaptation based on existing information in a weight of evidence approach	No, there is no reproductive toxicity evidence available from several independent sources of information or from the use of newly developed test methods.
Stage 3.1.4 – Adaptation based on non-animal approaches such as QSAR approaches and in vitro methods	No, the available Qualitative or Quantitative Structure-Activity Relationship (QSAR) and *in vitro* methods are currently not sufficient to address the complex endpoints on reproductive toxicity.
Stage 3.1.5 – Adaptation based on grouping and read-across	BDDGE (1,4-butanediol, reaction product with 1chloro-2,3-epoxypropane, EC Number 219-371-7) has been identified as a potential source of readacross information. No information regarding reproductive toxicity is available for BDDGE.
Stage 3.1.6 – Testing is technically not possible	No, the study is technically possible as it is possible to administer the registered substance orally.
Stage 3.1.7 – Substance-tailored exposure-driven testing	No, relevant human exposure cannot be excluded.
Stage 3.1.8 – Adaptation based on column 2 rules others than CMR classification	No, the substance is not of low biological activity, there is systemic absorption, and there is human exposure.

Stage 3.2 – Substances for which there are triggers for further information needs beyond the standard information requirements	No, there is no factor present in the existing toxicological database, whether based on theoretical substance specific scientific considerations or from experimental or observational data, that raises concerns that HDDGE may cause toxicity; but information is not comprehensive enough to allow a conclusion to be drawn.