What should we do if we manufacture an active substance using a fermentation process that uses peptones that are not of fish origin?

Answer:

You should include the following information in your CEP application:

- The origin of the peptone should be stated (e.g. animal or vegetable) and the sources should be identified (names and addresses of manufacturers);
- A control strategy discussion addressing the potential presence of histamine in the peptone (and hence in the active substance) should be provided;
- If the control strategy gives reassurance on the absence of histamine in the active substance, then the absence of a limit* in the active substance may be considered. Otherwise, a limit* for histamine should be included in the active substance

Any modification to the information provided on origin, source and limits will be subject to the requirements of the revision procedures for the CEP, and may require a revision to be submitted.

**This could be based on an acceptable intake of 2.1 µg/day, which is the reference level currently retained by the EMA Committee for Medicinal Products for Human Use (CHMP).*