What should we do if we manufacture an active substance using a fermentation process that uses materials of fish origin, including peptones?

Answer:

You should include the following information in your CEP application:

- The fish origin of the material should be stated and the sources identified (names and addresses of manufacturers);

For peptones or other material of fish origin:

- An appropriate limit* for histamine should be implemented in the specification of the peptone or material of fish origin;
- A limit* for histamine must be included in the specification of the active substance and will be reported on the CEP.

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, for example, 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).*

More information on this issue is available on the EMA website.