



CMC Review Memorandum

Date: October 31, 2018
To: The file STN 125563
From: Diana Kouliavskaia, OVRD/DVP, Product reviewer
Through: Steven Rubin, OVRD/DVP
Sara Gagneten, OVRD/DVP
Robin Levis, OVRD/DVP
Copy: Rana Chattopadhyay, OVRD/DVRPA, RPM
Applicant name: SANOFI PASTEUR SA
STN: 125563/0.34
Product: PR5I (Vaxelis)
Subject: Quality amendment to include updated Chemistry, Manufacturing and Controls (CMC) information on the IPV drug substance (multiple changes).
Action due date: December 29, 2018
Recommendation: Approval

Summary

Amendment STN 125563/0.34 was submitted to update the file with changes approved for IPOL vaccine for the drug substance manufactured with the same process (STN 103930). The changes related to CMC are reviewed below.

Also, proposed are two changes regarding the formulation of the trivalent IPV concentrate (Drug Substance) in (b) (4)) that are not reviewed in this review:

(b) (4)

Review of the changes

The company confirmed that there are no other changes than those declared in this submission.

The following changes are proposed to be included in the PR5I manufacturing process:

Change	Approval
(b) (4)	103930/5197
	103930/5197
	103930/5197
	103930/5197
	*
	103930/5219

(b) (4)	
	103930/5227
	103930/5221
	**
	103930/5195

* The supplement that this change was submitted to could not be located. Specification of (b) (4) (b) (4) is the current specification for IPOL DS intermediate (b) (4) and is proposed for the PR5I vaccine. This additional test will provide additional manufacturing quality assurance and is acceptable

** The supplement that this change was submitted to could not be located. This specification appears to be specific for the PR5I DS.

The company proposed to establish the End of shelf life (EoSL) specifications, which are based on the stability indicating parameters for the products. Release specifications, analytical methods, and associated validations remain unchanged.

- There is no difference in the EoSL specifications for the (b) (4) intermediate.
- For monovalent, new specification was established: (b) (4) compared to the result at release. This criterion was used in the studies of monovalent stability. In addition, release tests related to (b) (4) are not included in the EoSL specification as these tests are not relevant. There are no other differences between the release and EoSL specifications for monovalents.
- No differences between release and EoSL specifications for the Drug Substance (trivalent concentrate), with the exception of (b) (4) amount is tested at release and is not a stability indicating parameter.

Reviewer's Conclusion:

Most of the changes submitted by the company have been approved for the vIPV DS used in IPOL manufacture (STN 103930), and those that have not have been reviewed under that STN are acceptable. Proposed EoSL specifications for (b) (4) monovalents, and concentrated trivalent appear to be specific for the DS for PR5I, and are acceptable. The changes have been reviewed and determined to not impact product quality or safety.