

	Annual APIMF notification AAN	Immediate APIMF notification AIN	Minor amendment Amin	Major amendment Amaj
Change implementation	Prior acceptance not required To be notified within 12 months of implementation	Prior acceptance not required Change may be implemented immediately after notification of receipt has been received.	Can be implemented if WHO has not initiated correspondence with the applicant within 60 days ¹ of acknowledging receipt of amendment application.	Prior acceptance (signified by letter of acceptance) required.
WHO email to acknowledge receipt	30 days ¹ after receipt of application ²	7 days ¹ after receipt of application ²	7 days ¹ after receipt of application ²	7 days ¹ after receipt of application ²
Initial review by WHO	NA	If no objection raised within 45 days ¹ of date of acknowledgement of receipt of application can be considered accepted.	Within 60 days ¹ of date of acknowledgement of receipt of application.	Within 90 days ¹ of date of acknowledgement of receipt of application.
Additional data review by WHO	NA	NA	Within 45 days ¹ of date of receipt of response	Within 60 days ¹ of date of receipt of response
Additional criteria	<p>For multiple AAN changes for a given APIMF, the applicant should collate these in a single submission, or submit them in conjunction with submission of a revised APIMF version. Changes should be summarized in an amendment application form. Associated documentation (see guidance) should be available on request or inspection but does not need to be submitted, unless an AAN leads to a change in specifications or standard test procedures for the API or FPP. In this instance, a signed and dated version of revised specification and standard test procedures should be attached to the notification form, including a change history table.</p> <p>Normally no further communication with the applicant follows acknowledgement of receipt. However, if documentation is requested the applicant should submit this promptly. If the annual notification is rejected, the applicant must cease to apply the already implemented change(s), evaluate whether the change has an impact on the quality, safety or efficacy of the product, and take appropriate action with respect to any batches of the product already supplied, and notify WHO immediately.</p>	<p>If a notification is rejected, the applicant should cease to apply the rejected change(s) immediately.</p> <p>It is the responsibility of the applicant to evaluate whether the rejected change(s) has (have) an impact on the quality or safety of the API and to take appropriate action with respect to any batches of the API already supplied, and notify WHO immediately.</p>	<p>If the application does not meet requirements, but lacks only minor information or clarification, additional information or clarification may be requested. The applicant must not implement the change if such a request is made. Prior approval of the change is then required before implementation. A letter of acceptance, request for further information or rejection of the amendment will be issued within 45 calendar days of receipt of response.</p> <p>If the amendment requires an inspection of the manufacturing site, the change cannot be accepted until WHO GMP compliance has been confirmed.</p>	<p>If a manufacturing site inspection is required, the change cannot be accepted until WHO GMP compliance of the site has been confirmed.</p>

¹ Days equals calendar days.

² The amendment application cannot be considered to have been submitted until an email acknowledging receipt by WHO has been received. Such an email may take longer to receive for applications that are submitted during major holidays. (mainly Christmas, Easter or the month of August). Applicants who have not received an acknowledgement email within 10 days from the date of submission should contact WHO (prequalassessment@who.int).

Note: In exceptional situations, such as a request for approval of a complex grouping of changes, review time may be extended beyond the time specified above. If so, the anticipated WHO timeline will be communicated in the email acknowledging receipt of the submission