

	Annual notification AN	Immediate notification IN	Minor variation Vmin	Major variation Vmaj
Change Implementation	Prior acceptance not required To be notified within 12 months of implementation	Prior acceptance not required Change should be notified immediately after implementation	Can be implemented if WHO has not initiated correspondence with the applicant within 60 days of acknowledging receipt of application	Prior acceptance (signified by letter of acceptance) required
Who email to acknowledge receipt	45 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, the 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	Within 45 days ¹ of date of receipt of response ²	Within 45 days ¹ of date of receipt of response ²	Within 60 days ¹ of date of receipt of response ²
Additional criteria	<p>For multiple AN changes for a given FPP, the applicant should collate these in a single submission.</p> <p>Changes should be summarized in a variation application form. Associated documentation (see guidance) should be available on request or inspection but does not need to be submitted, unless an AN leads to a change in specifications or standard test procedures for the API or FPP. In this instance, signed and dated version of revised specification and standard test procedures should be attached to application 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 PQTm immediately.</p>	<p>Generally additional data are not requested although WHO may occasionally need to request further information. Such requests are generally communicated by email.</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, safety or efficacy of the FPP and to take appropriate action with respect to any batches of the FPP already supplied, and notify WHO immediately.</p>	<p>If the application does not meet requirements but lacks only minor information or clarification, additional information may be requested. Approval of the variation is then required before implementation. A letter of acceptance, request for further information or rejection of the variation will be issued within 45 calendar days of receipt of the response.</p> <p>If a variation refers to an APIMF, or a manufacturing site inspection is required, it cannot be accepted until the APIMF has been accepted, or the site's compliance with WHO Good Manufacturing Practices has been confirmed.</p>	<p>If a variation refers to an APIMF, or a manufacturing site inspection is required, it cannot be accepted until the APIMF has been accepted, or the site's compliance with WHO Good Manufacturing Practices has been confirmed.</p>

¹ Days equals calendar days.

² The variation 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 (prequalification@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 to the applicant by email.