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4 **Template for the Qualified Person's declaration**  
5 **concerning GMP compliance of the active substance**  
6 **used as starting material and verification of its supply**  
7 **chain "The QP declaration template"**  
8 **Draft**

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Comments should be provided using this [template](#). The completed comments form should be sent to [qwp@ema.europa.eu](mailto:qwp@ema.europa.eu)

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Keywords	<i>Qualified Person; Active Substance; Starting Material; good Manufacturing Practise; Supply Chain</i>
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12 **TEMPLATE FOR THE QUALIFIED PERSON'S DECLARATION**  
13 **CONCERNING GMP COMPLIANCE OF THE ACTIVE SUBSTANCE**  
14 **USED AS STARTING MATERIAL AND VERIFICATION OF ITS**  
15 **SUPPLY CHAIN "The QP Declaration Template"**

16 **1. ISSUE/OBJECTIVE**

17 The objective of this Qualified Person (QP) Declaration Template is to emphasise the importance of  
18 providing a comprehensive declaration, to harmonise the format for the declaration, to forestall  
19 questions during assessment, and to enhance the efficiency of the regulatory process.

20 The quality of medicinal products depends to a large degree on the quality of the active substances  
21 used to formulate them. Medicinal product manufacturers have the prime responsibility for ensuring  
22 the quality of active substances in terms of GMP compliance and prevention of falsification and should  
23 therefore take appropriate measures to:

- 24 (i) Verify the GMP compliance of all parties in the supply chain and that all sources are in  
25 accordance with relevant marketing authorisations.
- 26 (ii) Fully understand and control the supply chain of active substances used by them (including  
27 brokers, re-labellers and re-packagers) and take steps to shorten the supply chain wherever  
28 possible.
- 29 (iii) Clearly demonstrate that each batch of active substance accepted by them for use in the  
30 manufacture of medicinal products has been sourced through this supply chain.

31 In order to satisfy the above requirements, the manufacturer will submit a declaration that addresses  
32 GMP compliance and supply chain verification.

33 The attached QP declaration template provides, in a format considered suitable for submission, a basis  
34 for demonstrating compliance of the active substance manufacture with GMP requirements and that  
35 the manufacturer has relevant knowledge of the supply chain.

36 QP Declarations are required from each EEA finished product manufacturing site and/or from each site  
37 of importation/batch certification. However, a single declaration from one QP from one of the  
38 registered finished product or batch release sites may be sufficient, if its basis is satisfactorily  
39 described and supported by technical agreements between these sites (see Part B and E).

40 The QP Declaration should be provided in support of an application for a new marketing authorisation,  
41 variation or renewal of a medicinal product(s) authorised in the Community, using EU or national  
42 procedures within the scope of Directive 2001/83/EC<sup>1</sup> (human medicinal products) and Directive  
43 2001/82/EC<sup>2</sup> (veterinary medicinal products). A declaration is not required for blood or blood  
44 components; they are subject to the requirements of Directive 2002/98/EC<sup>8</sup>.

45 **2. REGULATORY BASIS**

46 **2.1 GMP compliance**

47 In accordance with Article 46(f) of Directive 2001/83/EC (human medicinal products) and Article 50(f)  
48 of Directive 2001/82/EC (veterinary medicinal products) as amended, Manufacturing Authorisation  
49 holders are required to use as starting materials only active substances which have been manufactured  
50 in accordance with the detailed guidelines on the Good Manufacturing Practice (GMP) for starting  
51 materials as adopted by the Community.

52 Confirmation of compliance is required for all applications for new marketing authorisations, renewals  
53 and for variations concerning a change (addition or replacement) to the registered manufacturer(s) of  
54 the active substance, finished product or batch importation/certification sites. For variations, the  
55 relevant legislative framework is provided by:- Commission Regulation (EC) No. 1234/2008 on  
56 variations<sup>3</sup> and Communication from the Commission - Guideline on the details of the various  
57 categories of variations to the terms of marketing authorisations for medicinal products for human use  
58 and veterinary medicinal products<sup>4</sup>.

59 Compliance for the above regulatory submissions is demonstrated by provision of *Qualified Person's*  
60 *Declaration Concerning GMP Compliance of the Active Substance Used as Starting Material and*  
61 *Verification of its Supply Chain* (i.e. the "QP declaration").

62 The QP Declaration should be based upon the direct audit of the active substance manufacturers, by or  
63 on behalf of the MAH, by a suitably trained and experienced person, which may be a third party  
64 contractor<sup>5, 6</sup>.

65 GMP certificates from a relevant Competent Authority cannot replace direct audits, but the results of  
66 such inspections may be used, together with other supporting information, in a risk-based approach by  
67 the manufacturer in establishing priorities for its own audit programme of active substance suppliers<sup>7</sup>.

## 68 ***2.2 Verification of the Active Substance supply chain traceability***

69 The supply chain is a family tree for the active substance tracing its history or supply chain from  
70 critical raw material(s) used in the manufacture of the active substance to the manufacturer of the  
71 dosage form. The sites will include manufacturers of critical raw materials (as defined in Part II of the  
72 EU GMP Guide 7.11, 7.13), active substance manufacturers, brokers, traders, repackers, relabellers,  
73 micronisers and importers.

74 This supply chain traceability should be established and documented. Verification of the availability of  
75 this forms part of the QP Declaration (Part D).

76 Supply chain traceability is considered a matter of GMP and it should be maintained by the  
77 Manufacturing Authorisation holder. This should be made available for inspection at the request of the  
78 competent authorities. Competent authorities need not be notified of amendments to the supply chain  
79 that are outside the scope of the Commission Regulation on variations<sup>4</sup>. Therefore, variations will only  
80 be required for changes to active substance manufacturers involved in the synthesis of the active  
81 substance from the designated starting materials to the final active substance as described in the  
82 marketing authorisation dossier Module 3.2.S.

## 83 **3. FORMAT AND GUIDANCE NOTES FOR THE QP** 84 **DECLARATION TEMPLATE**

85 The QP declaration provides the necessary information required to demonstrate compliance with Article  
86 46(f) of Directive 2001/83/EC and Article 50(f) of Directive 2001/82/EC that the Manufacturing  
87 Authorisation holder uses as starting materials only active substances which have been manufactured  
88 in accordance with the detailed guidelines on the Good Manufacturing Practice (GMP) for starting  
89 materials as adopted by the Community. Additionally, the QP declaration confirms the manufacturer  
90 has established a defined supply chain traceability for the active substance in compliance with Article  
91 46a of Directive 2001/83/EC and Article 50a of Directive 2001/82/EC, as amended. Verification of this  
92 is a requirement of the QP Declaration (Part D).

93 A QP declaration is required in support of a submission for a new marketing authorisation (MA)  
94 application, renewal or variation, for a human or veterinary medicinal product. As such, the QP

95 declaration will be accompanied by the relevant application form, which sets out the scope of the QP  
96 declaration and defines the applicable medicinal products.

97 The format of the QP declaration template is in five parts (Parts A to E) and each must be completed.  
98 In order for the QP declaration to be valid, all the relevant tick box(es) must be checked and the  
99 necessary information entered into the provided tables, as applicable. Guidance notes for completion of  
100 each section are provided below

## 101 **PART A: Concerned Manufacturing Sites**

102 This declares all the relevant sites that are subject to the QP declaration as applicable to the regulatory  
103 submission accompanying the QP declaration (i.e. a new MA, renewal or variation application). A  
104 decision tree for completion of Parts A and B of the QP declaration form is provided in Annex 1. The  
105 relevant sites and their respective functions are to be listed in the table provided according to the  
106 submission type, as shown below.

- 107 • For a new MA application: all proposed active substance / finished product (EEA and non-EEA)/  
108 importation / batch certification sites;
- 109 • For a Renewal: all currently approved active substance / finished product (EEA and non-EEA)/  
110 importation / batch certification sites;
- 111 • For a variation application to add a new finished product / importation / batch certification site:  
112 the proposed site and all currently approved active substance / finished product (EEA and non-  
113 EEA) / importation / batch certification sites;
- 114 • For a variation application to add a new active substance manufacturing site: the proposed site  
115 and all currently approved / finished product (EEA and non-EEA)/ importation / batch  
116 certification sites.

117 Note: According to the variation classification guideline<sup>4</sup>, currently approved active substance  
118 manufacturing site(s) for which valid QP declaration(s) is/are in place need not be listed in the table  
119 provided.

120 Optionally, the applicant may take the opportunity to include all currently registered active substance  
121 manufacturing sites in order to provide an updated QP declaration.

122 The following are taken into consideration in respect of the relevant sites that are listed in the table  
123 and which are subject of this QP declaration:

- 124 1. Batch certification can take place at the finished product manufacturer, at the importer (in the  
125 case of product manufactured in a third country) or at another EU site, if they hold an  
126 authorisation for batch certification.
- 127 2. No site may be exempted i.e. omitted from the table provided. Sites that are considered  
128 redundant should be deleted from the MA. Manufacturing sites that are located outside the EEA  
129 should be listed for transparency as this puts the QP declaration and arrangements for auditing  
130 within the context of the regulatory submission.

## 131 **PART B Declaration of GMP Compliance**

132 In this section the QP declares GMP compliance of the active substance manufacturer(s) and indicates  
133 whether a single or multiple declarations are provided covering all relevant manufacturing sites listed  
134 in PART A. A decision tree for completion of Parts A and B of the QP declaration form and identification  
135 of those cases where single or multiple declarations are required is provided in Annex 1.

136 In principle, individual declarations are expected from:

137 • The QP of each Manufacturing Authorisation holders (EEA) that use the active substance as a  
138 starting material

139 and

140 • The QP of each Manufacturing Authorisation holder responsible for importation / batch  
141 certification when the importation / batch certification site is a different site from the above.  
142 This is because the QP responsible for importation / batch certification takes overall  
143 responsibility for each batch.

144 Where more than one QP operates at a particular site, a declaration from one QP only is expected.

145 Thus in principle, multiple (individual) declarations are required covering all the relevant manufacturing  
146 (EEA) / importation / batch certification sites as listed in PART A that use the active substance as a  
147 starting material. However, a single declaration may be acceptable under certain circumstances.

148 In PART B, one of the following options must be completed as specified below by selecting the relevant  
149 tick-box. In each case, the QP signifies compliance with the requirements underpinning the declaration  
150 as set out in PART E.

151 **(i). Single declaration encompassing all relevant sites listed in PART A**

152 A single declaration signed by one QP may be acceptable in a situation where:-

153 • only one Manufacturing Authorisation is involved i.e. the product manufacturing site (EEA) /  
154 importation / batch certification sites are the same site or group of companies,

155 or

156 • more than one Manufacturing Authorisation holder is involved i.e. the product manufacturing  
157 site (EEA) / importation / batch certification sites are NOT the same site or group of  
158 companies. In this situation, the QP makes the declaration on behalf of all concerned QPs and  
159 confirms that this is underpinned by a technical agreement as set out in PART E.

160 Note:- where a single declaration is provided, only one completed QP declaration form is to be  
161 submitted.

162 **(ii). Multiple (individual) declarations covering all relevant sites listed in Part A**

163 Where it is not feasible to provide a single declaration covering all applicable finished product (EEA) /  
164 importation / batch certification sites where active substance is used as starting material, instead  
165 individual declarations may be submitted. In this case, the table provided should be completed to  
166 indicate those sites for which the QP is responsible for GMP compliance and is authorised to make the  
167 declaration.

168 Note:

169 1. There may be instances where it is possible to provide a single QP declaration for some  
170 manufacturing sites but individual declarations are required for other sites.

171 2. The Applicant is responsible for ensuring that that additional QP declaration forms have been  
172 provided to encompass all active substance / finished product (EEA ) / importation / batch  
173 certification sites as listed in PART A.

174 A covering note may be provided with the submission to confirm this.

175 **PART C Basis of the Declaration**

176 According to Directives 2001/83/EC and 2001/82/EC, as amended, and GMP requirements, it is  
177 expected that Manufacturing Authorisation holders will normally gain assurance that the active  
178 substance(s) used are manufactured in accordance with GMP through direct audit of the active  
179 substance manufacturer(s)<sup>5</sup>.

180 The arrangements for auditing that are applicable to the present QP declaration are indicated by  
181 completing sections (i), (ii) or (iii) as show below. In case of multiple active substance manufacturing  
182 sites as listed in PART A, the required information should be stated for all sites referred to in the  
183 regulatory submission.

184 Section (iv) enables supplementary information to be optionally submitted in support of the QP  
185 declaration.

186 PART C includes tick boxes that should be completed as confirmation that audit reports and other  
187 documentation pertaining to the audit are available for inspection by the Competent Authorities.

188 ***Section (i) audit conducted by Manufacturing Authorisation holder(s)***

189 Section (i) indicates that the Manufacturing Authorisation holder has conducted a direct audit of the  
190 active substance manufacturer(s). The table provided is completed to state those active substance  
191 manufacturing sites that have been audited by the Manufacturing Authorisation holder and the date of  
192 the last audit, which is expected to be within the last 3 years. Suitable justification should be provided  
193 in case the audit frequency exceeds 3 years.

194 ***Section (ii) audit conducted by third party***

195 Section (ii) indicates that an audit of the active substance manufacturing sites listed in the table  
196 provided has been conducted on behalf of the Manufacturing Authorisation holder by a suitably  
197 qualified third party (contractor). In this case, information should be provided as to who has conducted  
198 any audit(s) as appropriate e.g. third party including their relationships to Manufacturing Authorisation  
199 holder.

200 Tick boxes are completed to certify that the contract acceptors are properly qualified and that  
201 appropriate technical agreements are in place between the contract giver and acceptor.

202 ***Section (iii) evidence provided in lieu of audit***

203 Section (iii) should be completed only in exceptional circumstances where direct audit of the active  
204 substance manufacturer is not possible. In these circumstances, other arrangements for verifying the  
205 GMP status of the active substance manufacturer may be deemed acceptable. The relevant tick box is  
206 completed to indicate one of two possible scenarios, as applicable:

- 207
- 208 • remote assessment e.g. based on questionnaires and review of relevant documentation. This  
209 may be justified on grounds of current travel advice provided by the local authorities of the  
EEA member states;
  - 210 • other situations e.g. as applicable to non-traditional (or atypical) active substances.  
211 Appropriate elements of the EU GMP guide part II are nevertheless expected to be applied by  
212 the active substance and finished product manufacturers. As a principal, such controls must  
213 provide confidence that the 'Atypical' active substance is fit for purpose and will not negatively  
214 affect the safety and efficacy of the drug product. The QP is expected to justify the controls in  
215 place on a scientific basis and record a risk assessment on a product specific basis. Further  
216 guidance has been published<sup>9, 10</sup>.

217 In each of the above exceptional cases, an appropriate justification for the lack of an on-site audit  
218 should be provided together with a list of supporting information on which the verification of GMP  
219 compliance is based. The suitability of the justification provided may also be subject to review by the  
220 competent authority inspectors.

#### 221 ***Section (iv) supplementary supportive information (optional)***

222 Section (iv) refers to supplementary information that may optionally be attached to the QP declaration  
223 to support a risk-based approach by the manufacturer in establishing priorities for its own audit  
224 programme. For example, results of inspection report(s) or GMP certificate(s) issued by EEA, Mutual  
225 Recognition Agreement (MRA) partners or other recognised authority together with other supporting  
226 information. The table provided should be completed to summarise the information that has been  
227 provided. It should be noted however that this supporting information alone cannot fulfill the statutory  
228 obligations of the Manufacturing Authorisation holder or the requirements of section 5.25 of the GMP  
229 Guide. Further guidance is available<sup>7, 11</sup>.

### 230 **PART D Verification of the active substance supply chain traceability**

231 This section declares three key aspects of the defined supply chain for each of the active substance  
232 manufacturing sites listed in PART A i.e. that:-

- 233 (i) the supply chain had been established and is documented
- 234 (ii) there exists a documented risk assessment for all sites in the supply chain
- 235 (iii) the above documents are available for inspection

### 236 **PART E Attestation of the responsible QP**

237 This declares that the signatory is the QP responsible for the relevant product manufacturer(s) (EEA)  
238 and importation and/or batch certification sites referenced in PART B.

239 Applicants are reminded that, according to Art. 41 of Directive 2001/83/EC and Article 45 of Directive  
240 2001/82/EC, Manufacturing Authorisation holders shall have at their disposal at least one Qualified  
241 Person located in the EEA. Therefore declarations from persons employed by manufacturers in third  
242 countries, including those located within MRA partner countries, are not acceptable. The latter may,  
243 however be used to provide supportive information for the QP declaration – see PART C (iv).

244 This section also sets out the requirements in situations where a declaration covers multiple sites listed  
245 in PART A and the QP confirms that appropriate technical agreements are in place between  
246 sites/companies concerning GMP compliance. It is expected that arrangements concerning GMP of the  
247 active substance between companies are underpinned by agreement/procedures irrespective of  
248 whether the companies are within the same group or not.

249 The declaration is signed and the relevant details of the QP are provided (name, status, and  
250 Manufacturing Authorisation holder name and number). The QP details should be consistent with those  
251 named within the relevant regulatory submission application form and/or the Manufacturing  
252 Authorisation.

253 **References:**

254 1. Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the  
255 Community code relating to medicinal products for human use (Consolidated version :  
256 05/10/2009).

257 <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:2001L0083:20091005:EN:PDF>

258 2. Consolidated Directive 2001/82/EC of the European Parliament and of the Council of 6 November  
259 2001 on the Community code relating to veterinary medicinal products as amended by Directive  
260 2004/28/EC

261 [http://ec.europa.eu/health/files/eudralex/vol-5/consol\\_2004/dir\\_2001\\_02-dir\\_2004\\_28-cons\\_en.pdf](http://ec.europa.eu/health/files/eudralex/vol-5/consol_2004/dir_2001_02-dir_2004_28-cons_en.pdf)

262 3. Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of  
263 variations to the terms of marketing authorisations for medicinal products for human use and  
264 veterinary medicinal products (Official Journal L 334, 12/12/2008 p. 7 - 24).

265 [http://ec.europa.eu/health/files/eudralex/vol-1/reg\\_2008\\_1234/reg\\_2008\\_1234\\_en.pdf](http://ec.europa.eu/health/files/eudralex/vol-1/reg_2008_1234/reg_2008_1234_en.pdf)

266 4. Communication from the Commission — Guideline on the details of the various categories of  
267 variations to the terms of marketing authorisations for medicinal products for human use and  
268 veterinary medicinal products (2010/C 17/01)

269 [http://ec.europa.eu/health/files/eudralex/vol-2/c17\\_1/c17\\_1\\_en.pdf](http://ec.europa.eu/health/files/eudralex/vol-2/c17_1/c17_1_en.pdf)

270 5. European Medicines Agency: Inspections: Q&A: Good Manufacturing Practice (GMP)

271 EU GMP guide part II Basic requirements for active substances used as starting materials: GMP  
272 compliance for active substances

273 Q1: How can GMP compliance for active substance manufacturers be demonstrated?

274 [http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q\\_and\\_a/q\\_and\\_a\\_detail\\_000027.js](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000027.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800296ca&jsenabled=true)  
275 [p&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800296ca&jsenabled=true](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000027.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800296ca&jsenabled=true)

276 6. European Medicines Agency: Inspections: Q&A: Good Manufacturing Practice (GMP)

277 EU GMP guide part I Basic requirements for medicinal products: Chapter 5 Qualification of  
278 suppliers.

279 Q1 Is an audit performed by a third party acceptable?

280 [http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q\\_and\\_a/q\\_and\\_a\\_detail\\_000027.js](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000027.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800296ca&jsenabled=true#section10)  
281 [p&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800296ca&jsenabled=true#section10](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000027.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800296ca&jsenabled=true#section10)

282 7. European Medicines Agency: Inspections: Q&A: Good Manufacturing Practice (GMP)

283 EU GMP guide part II Basic requirements for active substances used as starting materials: GMP  
284 compliance for active substances

285 Q2: Do I need to perform an audit of an active substance supplier if it has been inspected by an  
286 inspectorate from an EEA member state and a valid GMP certificate is available?

287 [http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q\\_and\\_a/q\\_and\\_a\\_detail\\_000027.js](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000027.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800296ca&jsenabled=true)  
288 [p&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800296ca&jsenabled=true](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000027.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800296ca&jsenabled=true)

289 8. Directive 2002/98/EC of the European Parliament and of the Council of 27 January 2003 setting  
290 standards of quality and safety for the collection, testing, processing, storage and distribution of



291 human blood and blood components and amending Directive 2001/83/EC (Official Journal L 33,  
292 8/2/2003 p. 30 - 40).

293 [http://ec.europa.eu/health/files/eudralex/vol-1/dir\\_2002\\_98/dir\\_2002\\_98\\_en.pdf](http://ec.europa.eu/health/files/eudralex/vol-1/dir_2002_98/dir_2002_98_en.pdf)

294 9. European Medicines Agency: Inspections: Q&A: Good Manufacturing Practice (GMP)

295 EU GMP guide part II Basic requirements for active substances used as starting materials: GMP  
296 compliance for active substances

297 Q6: The Notice to Applicants requires the submission of a declaration signed by the Qualified  
298 Person that the active substance used is manufactured in accordance with GMP. The active  
299 substance in my product is widely used, but not normally as a pharmaceutical active substance,  
300 and I am having some difficulty in confirming compliance. What should I do to furnish the  
301 required declaration?

302 [http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q\\_and\\_a/q\\_and\\_a\\_detail\\_000027.js  
303 p&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800296ca&jsenabled=true](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000027.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800296ca&jsenabled=true)

304 10. Medicines and Healthcare products Regulatory Agency (MHRA):

305 Active Pharmaceutical Ingredients (API):

306 Good Manufacturing Practice (GMP) expectations for Active Pharmaceutical Ingredients (APIs)

307 GMP expectations of Non Traditional APIs

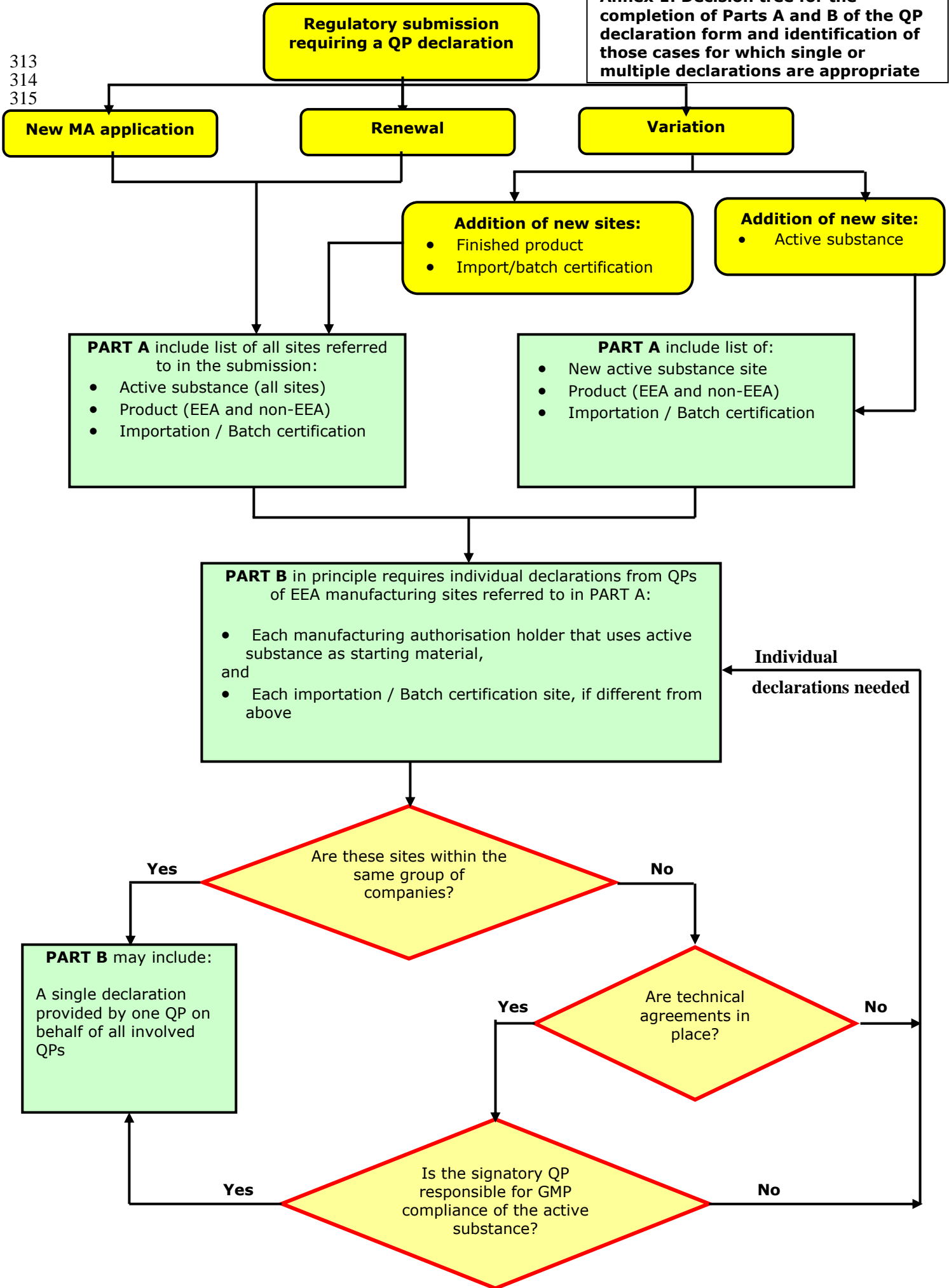
308 [http://www.mhra.gov.uk/Howweregulate/Medicines/Inspectionandstandards/GoodManufacturingPractic  
309 e/Guidanceandlegislation/ActivePharmaceuticalIngredientsAPI/index.htm](http://www.mhra.gov.uk/Howweregulate/Medicines/Inspectionandstandards/GoodManufacturingPractice/Guidanceandlegislation/ActivePharmaceuticalIngredientsAPI/index.htm)

310 11. European Medicines Agency: Inspections: Mutual Recognition Agreements

311 [http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document\\_listing/document\\_listing\\_  
312 000248.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac058005f8ac](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000248.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac058005f8ac)

313  
314  
315

**Annex 1: Decision tree for the completion of Parts A and B of the QP declaration form and identification of those cases for which single or multiple declarations are appropriate**



**QUALIFIED PERSON'S DECLARATION CONCERNING GMP COMPLIANCE OF THE ACTIVE SUBSTANCE USED AS STARTING MATERIAL AND VERIFICATION OF ITS SUPPLY CHAIN**  
**"The QP Declaration Template"**

**PART A: Concerned Manufacturing Sites**

I confirm that all sites concerned with manufacture of the active substance *[insert name of active substance]*, and finished product and importation and/or batch certification for product(s) defined in the accompanying application form for the MA application/renewal/variation *[delete as applicable]*, are stated below, as applicable.

<b>MANUFACTURING SITES SUBJECT OF THIS DECLARATION<sup>1</sup></b>		
<b>ACTIVE SUBSTANCE MANUFACTURING SITE <sup>2, 3</sup> AND FUNCTION(S)</b>	<b>FINISHED PRODUCT MANUFACTURING SITE(S) AND FUNCTION(S)</b>	<b>IMPORTATION AND/OR BATCH CERTIFICATION SITE</b>

1 Where the Applicant has multiple sites for the manufacture of active substance, product or importation and/or batch certification, the QP declaration shall encompass all these sites, as applicable to the regulatory submission defined in the accompanying application form.

No site may be exempted from this list.

All sites concerned with part processing should be listed.

2 State the site name and address in detail, including the building numbers and function.

This information may additionally be provided in a flow chart for clarity.

3 List each site involved in the synthesis of the active substance beginning with the introduction of the designated active substance starting material.

335 **PART B: Declaration of GMP Compliance**

336 I declare that **[insert name of active substance]** used as starting material in the manufacture of  
337 product as defined in the accompanying application form and in PART A of this QP declaration, is  
338 manufactured in accordance with the detailed guideline on good manufacturing practice for active  
339 substances used as starting materials as required by Article 46(f) of Directive 2001/83/EC and Article  
340 50(f) of Directive 2001/82/EC, as amended. This declaration is underpinned by requirements as set out  
341 in PART E and is provided as follows:

342 Please tick and complete only one of the following options, either (i) or (ii), as applicable

343  **(i). Single declaration encompassing all relevant sites listed in PART A**

344 A single declaration signed by one QP is provided covering all applicable active substance / finished  
345 product (EEA)/ importation / batch certification sites as listed in PART A.

346 **or**

347  **(ii). Multiple (individual) declarations covering all relevant sites listed in PART A**

348 It is not feasible to provide a single declaration covering all applicable finished product (EEA) /  
349 importation / batch certification sites where active substance is used as starting material.

350 Instead, individual declarations are submitted from each of the manufacturing sites listed in PART A.

351 This QP declaration covers the manufacturing sites listed below that use active substance as starting  
352 material.

NAME OF ACTIVE SUBSTANCE MANUFACTURING SITE(S)	NAME OF PRODUCT MANUFACTURING (EEA) /IMPORTATION/BATCH CERTIFICATION SITE(S)	MANUFACTURING / IMPORTATION AUTHORISATION NUMBER (MIA)

353

354 **PART C: Basis of the Declaration**

355 **I declare that:**

356 GMP compliance of the manufacturer(s) of the active substance **[insert name of active substance]**  
357 listed in PART A has been verified on the basis of (i) or (ii) or (iii) – one of these sections should be  
358 completed. Additional supporting information may optionally be included in section (iv).

359 and

360 Audit report(s) and other documentation relating to the audit(s) of the active substance  
361 manufacturer(s) listed in PART A are in place and will be made available for inspection by the  
362 competent authorities if requested.

363 Please tick and complete each section, as applicable

364  **(i) Audit of the active substance manufacturer(s) conducted by Manufacturing**  
365 **Authorisation holder(s):**

366 Audit(s) of the active substance manufacturer(s) listed in PART A relative to the product stated in this  
367 declaration has/have been completed by the Manufacturing Authorisation holder as listed below and all  
368 critical concerns have been rectified:

<b>Name of active substance manufacturer</b>	<b>Name of Manufacturing Authorisation holder (or corporate representative, within the same group of companies) having conducted the audit</b>	<b>Date of last audit<sup>4</sup></b>

369 4 Justification should be provided below if the date of last inspection exceeds 3 years:

370  **(ii) Audit of the active substance manufacturer(s) conducted by third party**

371 Audit(s) of the active substance manufacturer(s) listed in PART A relative to the product(s) stated in  
372 this declaration has/have been completed by the third party auditing body(ies) i.e. contract acceptor(s)  
373 on behalf of the Manufacturing Authorisation holder(s) i.e. contract giver(s) as listed below and all  
374 significant corrective actions have been completed:

<b>Name of active substance manufacturer</b>	<b>Auditing body (contract acceptor)</b>	<b>Name of Manufacturing Authorisation holder (contract giver)</b>	<b>Date of audit (completion)<sup>4</sup></b>

375 4 Justification should be provided below if the date of last inspection exceeds 3 years:

376 and,

377 **I declare that:**

378  (i) I have evaluated each of the named contract acceptor(s) in respect of the above  
379 audit(s). The audit(s) was/were conducted by properly qualified and trained staff, in  
380 accordance with approved procedures.

381 and,

382  (ii) Technical contractual arrangements are in place and that any measures taken by the  
383 contract giver(s) are documented e.g. signed undertakings by the auditor(s).

384  **(iii) Evidence provided in lieu of audit**

385 Exceptionally, and if satisfactorily justified, other supporting evidence used in lieu of an on-site audit of  
386 the active substance manufacturer(s) by the manufacturer(s).

387 Please tick and complete the applicable section and provide appropriate supporting information:

388  Remote assessment based on, for example, questionnaires, review of documents, ISO 9000  
389 certification, results of analytical testing and historical experience with the supplier.

390 The justification for this approach is attached.

391 Or

392  Other situations e.g. Non Traditional (or Atypical) Active Substance

393 The justification for this approach is attached (see guidance notes).

394 **(iv) Supplementary supportive information (optional):**

395 For the active substance manufacturing sites listed below results of inspection report(s) or GMP  
396 certificate(s) issued by EEA, MRA partners or other recognised authority together with other supporting  
397 information are attached.

Name of active substance manufacturer	Summary of supporting information provided

398 **PART D: Verification of the Active Substance supply chain traceability**

399 ***I declare that:-***

400 (i) the active substance supply chain of each of the active substance manufacturing sites listed in  
401 Part A has been established and documented.

402 and,

403 (ii) there exists a documented risk assessment for all sites in the supply chain of the active  
404 substance.

405 and,

406 (iii) the above documents are available for inspection.

407 **PART E: Attestation of the responsible QP**

408 This section declares that the signatory is the QP responsible for the relevant product manufacturer(s)  
409 (EEA) and importation and/or batch certification sites as referenced in PART B.

410 **I confirm that:**

- 411 (a) I am a QP with responsibility for GMP compliance of the active substance and am authorised to  
412 make this declaration;
- 413 (b) In the case of multiple sites as specified in PART B, this declaration is made on behalf of all the  
414 involved QPs named on the relevant Manufacturing Authorisation(s)
- 415 (c) the arrangements are underpinned by a technical agreement as described in Chapter 7 of the  
416 GMP Guide, as applicable;
- 417 (d) a documented procedure defining GMP responsibilities is in place and that  
418 arrangements/agreements exist between the named companies concerning management of  
419 GMP responsibilities;
- 420 (e) the relevant technical agreements and procedures are available for inspection by the  
421 competent authorities.

422 This declaration is submitted by:-

Signatory _____  Print name _____  Date _____	Status (job title) _____  Manufacturing Authorisation name: _____  Manufacturing Authorisation number: _____
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