Screening Checklist for Biotherapeutic Products and their corresponding SBPs

 Full pathway

# Part A – Administrative Information (WHO Guidelines on submission of documentation for the pilot procedure for prequalification of similar biotherapeutic products for rituximab and trastuzumab - Preparation of product dossiers in common technical document format)

**Similar Biotherapeutic Product (SBP) information**

|  |  |  |
| --- | --- | --- |
| **Dossier screening #** | **Applicant short name** | **Submission date** |
|  |  |  |
| **Screening date** | **Recommendation** |
|  |  |
| **Is the application for SBPs for rituximab or trastuzumab that have been registered by non-SRAs ?** |
|  |
| **Is the reference biotherapeutic product (RBP) approved by an SRA?** (If not: **STOP SCREENING** and comment) |
|  |
| **Are the RBP batches used to generate the required similarity evidence been obtained/purchased from an SRA country?** (If not: **STOP SCREENING** and comment) |
|  |
| **Strength** |
|  |
| **Packaging and pack size** |
|  |
| **Is the product strength invited (listed in EOI)?** (If not: **STOP SCREENING** and comment – note that some manufacturers may be claiming as a strength a nominal fill amount rather than what is delivered from the presentation. This should not result in outright rejection of the dossier but for a clarification).The naming of the product strength should be in the form indicated in the EOI. |
|  |
| **Is the SBP marketed in the Country of registration?** (If not: **STOP SCREENING** and comment)  |
|  |
| **Information regarding any other related dossiers (e.g. DP(s) with the same DS submitted to the Prequalification Team: medicines (PQTm) by the applicant):** |
|  |
| **Packaging, pack sizes and shelf life** for each different packaging format |
|  |
| **Is the candidate product’s indication the same as per RBP SmPC?** |
|  |
| **Is the Application correctly applying for the full assessment pathway (i.e. or is there an indication the product was accepted by an SRA and is currently on the SRA market)?** |
|  |
| **Has a covering letter been submitted, expressing interest in participating in the WHO prequalification procedure and confirming that the information submitted in the product dossier is complete and correct?** |
|  |
| **Name of the applicant and official address (must be in English)** |
|  |
| **Is the applicant also the manufacturer of the Drug Product?** **If it is not, is supporting documentation provided including a signed document of the division of responsibilities and a demonstration that the applicant is in full control of the manufacturing process?**  |
|  |
| **Proprietary name of the drug product (DP) (if applicable)** |
|  |
| **INN of drug substance (DS)** |
|  |
| **Names of all proposed DS manufacturers, physical address(es) of manufacturing site(s) (and unit if applicable), including intermediates, contractors and release testing (indicate function of each site)** |
|   |
| **Is a site master file (SMF) for each manufacturing site (DS) listed in the product dossier present?**  |
|  |
| **Names of all proposed manufacturers of DP, physical address(es) of manufacturing site(s) (and unit if applicable), including intermediates, primary packaging site and release testing (indicate function of each site)** |
|   |
| **Is a site master file (SMF) for each manufacturing site (DP) listed in the product dossier present?**  |
|  |
| **Clinical site listed in the product dossier** |
|   |
| **Has a contract research organization master file (CROMF) been provided for each clinical site listed in the product dossier, in the format specified in the WHO guidance documents for submitting a CROMF?** |
|   |
| **RBP, name of marketing holder and manufacturers**  |
|  |
| **Stringent regulatory authority that approved the RBP**  |
|  |
| **Is information on the market where the RBP was purchased present?** |
|  |
| **Format of submission** – confirm Common Technical Document format |
|  |
| **Has all documentation been submitted in English and includes officially certified English translations of product information and other documents, if applicable. In the case of English translations, has the English language version of the product information also been submitted as Word files?** |
|  |
| **Full name of applicant and official address** |
|  |
| **Name, title and contact details of the designated contact person** |
|  |

# Part B – Document required by WHO Guidelines on submission of documentation for Full pathway

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Information required****(please comment below, if requirements not fully met)** | **YES** | **NO** |
|  |  1 | Is a list of the manufacturer(s) of the drug product (DP), including manufacturers of intermediates, primary packaging sites and release-testing sites, with the physical address of the manufacturing site(s) (and unit if applicable) been provided? |  |  |
|  | Comment |  |
|  |  2 | Is a list of manufacturer(s) of the Drug substance (DS) used in the manufacture of the DP, with the physical address of the manufacturing site(s) (and unit if applicable) present? |  |  |
|  | Comment |  |
|  | 3 | Does the applicant indicate the full physical address of the DP/DS manufacturing site including Unit and Block numbers, where applicable?  |  |  |
|  | Comment |  |
|  | 4 | Has the applicant submitted valid manufacturing licenses and/or valid Good Manufacturing Practice certificates for all the DP and DS manufacturers?  |  |  |
|  | Comment |  |
|  | 5 | If the DS manufacturing site is not part of the same pharmaceutical group as the DP manufacturer, has a declaration been provided from the DS manufacturer that:a. it has provided to the DP manufacturer all confidential and non-confidential information regarding the preparation, control and stability of the DS as per ICH module 3.S.2; and,b. it will inform the DP manufacturer of any changes to the preparation, control and stability of the DS? |  |  |
|  | Comment |  |
|  | 6 | Is the demonstration of similarity between an SBP and RBP based on scientific evidence and a comprehensive similarity exercise? |  |  |
|  | Comment |  |
|  | 7 | Does CTD Module 3 contain similarity exercise with relevant discussion in section 3.2.R? |  |  |
|  | Comment |  |
|  | 8 | Does the SBP biosimilarity data set include clinical, validation and commercial batches? |  |  |
|  | Comment |  |
|  | 9 | Has the applicant submitted documentation regarding the purchase, shipping, and storage of the comparator product used in the comparability and similarity exercise (quality, non clinical and clinical)? |  |  |
|  | Comment |  |
|  | 10 | Has the applicant submitted the Quality Overall Summary – Biotherapeutic Product (QOS-BTP) as Word document using the most recent version? |  |  |
|  | Comment |  |
|  | 11 | Has the QOS template been altered (missing sections, subsections, tables, etc)? |  |  |
|  | Comment |  |
|  | 12 | Is the QOS-BTP completed in an acceptable way, including references to dossier volumes and pages? |  |  |
|  | Comment |  |
|  | 13 | Does the data submitted include data on similarity of the SBP to an SRA-approved RBP in terms of quality characteristics, biological activity, safety and efficacy? |  |  |
|  | Comment |  |
|  | 14 | Does the product dossier contain comprehensive data on quality, nonclinical and clinical parameters? |  |  |
|  | Comment |  |
|  | 15 | Does the product dossier contain PK/PD pivotal clinical studies?  |  |  |
|  | Comment |  |
|  | 16 | Does the product dossier contain safety/efficacy clinical studies?  |  |  |
|  | Comment |  |
|  | 17 | Is evidence provided of compliance with WHO’s recommended standards for good clinical practice (GCP)? |  |  |
|  | Comment |  |
|  | 18 |  Is evidence provided of compliance with WHO’s recommended standards for good distribution practices (GDP)? |  |  |
|  | Comment |  |
|  | 19 | Is evidence provided of compliance with WHO’s recommended standards for good manufacturing practices (GMP)? |  |  |
|  | Comment |  |
|  | 20 | Is evidence provided of compliance with WHO’s recommended standards for good laboratory practices (GLP)? |  |  |
|  | Comment |  |
|  | 21 | At the time of submission, is the stability data provided for the **bulk DS** (in case bulk material is to be stored after manufacture but prior to formulation and final manufacturing) for at least 6 months in cases where storage periods greater than 6 months are requested? [*at least 3 batches for which manufacture and storage are representative of the manufacturing scale of production*] |  |  |
|  | Comment |  |
|  | 22 | At the time of submission, is the stability data provided for the **DP** (final container product representative of that which will be used at manufacturing scale) for at least 6 months in cases where storage periods greater than 6 months are requested? [*at least 3 batches for which manufacture and storage are representative of the manufacturing scale of production*]? |  |  |
|  | Comment |  |
|  | 23 | If contract manufacturing is involved, are the responsibilities of all parties clearly defined?  |  |  |
|  | Comment |  |
|  | 24 | If technology transfer is involved, has validation data been presented?  |  |  |
|  | Comment |  |
|  | 25 | Is there data or a protocol presented for prospective validation of 3 consecutive production scale batches (of the largest proposed production size)? |  |  |
|  | Comment |  |
|  | 26 | Does the manufacturer include in Section 2.3.R copies of executed production records for the batch(es) used in the comparability study and proposed blank master production record(s) for proposed production batch(es)?  |  |  |
|  | Comment |  |
|  | 27 | Is validation data provided for all analytical methods referenced in the specification of DS and DP? |  |  |
|  | Comment |  |
|  | 28 | Have the qualified analytical methods been verified? |  |  |
|  | Comment |  |
|  | 29 | Is there data on DS and DP batch sizes and composition of pilot and production scale as well as those used in comparability and similarity exercise (quality, non clinical and clinical)? |  |  |
|  | Comment |  |
|  | 30 | Does the dossier contain a tabular overview of DS and DP development batches, including process changes, pilot and production scale batches as well as those used in comparability and similarity exercise (quality, non clinical and clinical)? |  |  |
|  | Comment |  |
|  | 31 | Is proposed product information (summary of product characteristics (SmPC), or an equivalent thereof, the patient information leaflet (PIL), or equivalent thereof, and the labelling) of the product present?  |  |  |
|  | Comment |  |
|  | 32 | Is a statement present indicating that the product is actually on the market of the registration country or region?  |  |  |
|  | Comment |  |
|  | 33 | Is a copy of the marketing authorization, or the equivalent thereof, issued by the registration country or region to demonstrate that the product is registered or licensed in accordance with registration country or region’s requirements present? If applicable, a copy of the latest renewal of the marketing authorization should also be provided (comment) |  |  |
|  | Comment |  |
|  | 34 | Is a rationale provided for the choice of the SRA-licensed RBP by the manufacturer of the SBP that takes in consideration the RBP’s quality, efficacy and safety in a given population? |  |  |
|  | Comment |  |
|  | 35 | Is evidence provided that the selected RBP has been licensed and approved by an SRA based on a product dossier containing comprehensive data on non-clinical and clinical studies and full quality, safety and efficacy data? |  |  |
|  | Comment |  |
|  | 36 | Has a copy of the current DP specifications (release and shelf-life), dated and signed or certified by authorized personnel, with the analytical test procedures been provided? |  |  |
|  | Comment |  |
|  | 37 | Is a tabular listing of the product batches manufactured for the market of registration region or country since approval or during the past five years, whichever is shorter, been provided? [*The table should include at least the following information: the batch number (of both the DS and DP), batch size (number of units), date of manufacture, manufacturing site (of both the DS and DP), expiry date and pack type/size*]  |  |  |
|  | Comment |  |
|  | 38 | Has a copy of the most recent product quality review, prepared according to WHO requirements been provided [*according to WHO Technical Report Series No. 986, 2014*]?  |  |  |
|  | Comment |  |
|  |  39 | Are safety specification, pharmacovigilance plan, risk management plan and post-marketing safety reports provided? [according to the WHO Guidelines on evaluation of SBPs/BTPs or the WHO Guidelines on the quality, safety and efficacy of biotherapeutic protein products prepared by recombinant DNA technology] |  |  |
|  | Comment |  |
|  |  40 | Does the RMP include a description of the risks of the product together with the measures to minimize such risks, taking into consideration patient treatment and current clinical practice in low- and middle-income countries and for supply of the product based on its prequalification status? |  |  |
|  | Comment |  |
|  |  41 | Has a Qualified Person Responsible for Pharmacovigilance (QPPV) been identified? Have contact details, role and responsibility been detailed? |  |  |
|  | Comment |  |
|  |  42 | Are post marketing safety reports provided from date of marketing approval to present? |  |  |
|  | Comment |  |
|  |  43 | Have the arrangements been described for handling complaints and product recalls used for supply of the product based on its prequalification status, including provisions for informing WHO and the procurement agencies? |  |  |
|  | Comment |  |
|  |  44 | Have restrictions been described for procedures on distribution or recalls, including manufacturer-initiated recalls? |  |  |
|  | Comment |  |
|  | 45 | Is a sample(s) of the product in market packaging(s) with the respective certificate of analysis provided? [This should be provided with the submission to enable visual inspection thereof. No special transportation is required for the samples for the purpose of this requirement].  |  |  |
|  | Comment |  |
|  | 46 | Has evidence been provided that the product will - prior to – and at the time of packing –be kept within the storage temperature limits recommended by the manufacturer?   |  |  |
|  | Comment |  |
|  | 47 | Are the shipment and transportation validation studies in line with the principles laid out in the WHO guideline for international packaging and shipping of vaccines?[shipping validation at an ambient temperature of 43°C minimum (for at least 48 hours), as already established in the WHO guideline for international packaging and shipping of vaccines]?**If NO** please respond to question 48 |  |  |
|  | Comment |  |
|  | 48 | **If point 47 answer is NO:** If the applicant followed a different approach, are the differences justified and the equivalence of the approach discussed and supported by data? Data expected for the assessment includes a summary of the packaging procedures for international shipments (including box sizes and types, packing volumes, etc.), and the validation protocols and reports of the shipping boxes used for supply of the product based on its prequalification status? |  |  |
|  | Comment |  |
|  | 49 | Is evidence provided of adherence to the principles laid out in the WHO guidelines on the international packaging and shipping of vaccines? |  |  |
|  | Comment |  |
|  | 50 | Has the CTD been submitted in Microsoft Word or text-selectable PDF format? |  |  |
|  | Comment |  |
|  | 51 | Does CTD Module 1 contain documents specific to WHO; for example, application forms or the proposed label for use in the region? |  |  |
|  | Comment |  |
|  | 52 | Does CTD Module 1 contain a summary of the similarity information? |  |  |
|  | Comment |  |
|  | 53 | Does CTD Module 1 contain the list the countries in which the marketing authorization for the SBP has been granted, rejected or withdrawn? |  |  |
|  | Comment |  |
|  | 54 | Does CTD Module 1 contain the regional summaries? |  |  |
|  | Comment |  |
|  | 55 | Does CTD Module 1 contain labelling/draft labelling according to the information on WHO public assessment reports (WHOPARs)? |  |  |
|  | Comment |  |
|  | 56 | Does CTD Module 3 contain Information on manufacturing and quality? |  |  |
|  | Comment |  |
|  | 57 | Does CTD Module 4 contains nonclinical study reports? |  |  |
|  | Comment |  |
|  | 58 | Does CTD Module 5 contains human study reports and related information (PK/PD pivotal clinical studies and clinical safety/efficacy studies)? |  |  |
|  | Comment |  |
|  | 59 | Is the Adventitious Agents Safety Evaluation present in module 2.3.A.2 ? |  |  |
|  | Comment |  |
|  | 60 | Additional requirements for Sterile DP are met? (see Part C)?  |  |  |
|  | Comment |  |

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| **Comments on deficiencies****with reference to table above and specific dossier sections** |
| **Additional data requested**(to be communicated to the applicant) |
|  |

# Part C – Sterile Aspects

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| --- |
| **Sterile aspects** |
| 1. Manufacturing process validation data including media fill results from a recent media fill exercise/study for the aseptic process at the DP manufacturing site is submitted?
 |  |
| Comment:  |
| 1. Suitability of container closure — compatibility with DS/DP, demonstration of seal integrity (e.g. by microbial ingress test, dye ingress test), suitability for transportation to DP site etc. provided?
 |  |
| Comment:  |
| 1. Rubber stoppers/gasket: Supplier name, type and stopper number; evidence of physicochemical testing as per USP <381> and its physiological safety as per USP < 87>/<88>) or other equivalent requirements. Attestation from the supplier that the closure is free of 2-mercapto benzothiazoles (2-MCBT) and nitrosamines; compatibility with DS/DP(e.g. leachables/ extractables). Provided?
 |  |
| Comment:  |
| 1. Transportation studies — to demonstrate mode of transport chosen is appropriate (e.g. through simulation). Provided?
 |  |
| Comment:  |
| 1. A copy of blank and executed batch manufacturing record (BMR) including copies of all standard operating procedures (SOPs) pertinent to: *sterilization of manufacturing equipment, packaging materials and accessories; aseptic procedures + media fill exercises; in-process controls*. Provided?
 |  |
| Comment: |
| 1. Filters: Make/type, article number and/or code, suppliers, filter validation data (e.g. compatibility with the DS/DP, leachables/extractables, microbial retention for sterilizing filters etc.). Provided?
 |  |
| Comment: |
| 1. Description of manufacturing process/flow diagram: Environmental conditions in the manufacturing, filling and packaging areas (temperature, pressure, grades of area class etc.). Provided?
 |  |
| Comment:  |
| 1. Evidence of validation of the conditions/parameters used for the sterilization/depyrogenation of the processing equipment and accessories, filters and packaging components. Provided?
 |  |
| Comment:  |
| 1. Stability data generated using samples stored in inverted orientation where rubber closures are used. Provided?
 |  |
| Comment:  |

|  |
| --- |
| **Comments on deficiencies****with reference to table above and specific dossier sections** |
| **Additional data requested**(to be communicated to the applicant) |
|  |