Frequently Asked Questions: Control of Active Pharmaceutical Ingredients (API).

NO.	QUESTION	ANSWER
1.	**What is the definition of API**	Any substance or mixture of substances intended to be used in the manufacture of a pharmaceutical dosage form and that, when used, so becomes an active ingredient of that pharmaceutical dosage form. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease of disease or to affect the structure and function of the body (World Health Organization (WHO)).
2.	**What can be classified under API?**	API can be divided into; • Inorganic substance • Organic substances (isolated from material of animal or human origin) • Organic substances (synthetic or semi-synthetic or isolated from herbal sources or micro-organism)
3	**Why the NPCB needs to control API?**	Mandatory control of API can reduce the risk of sourcing substandard or contaminated materials to ensure a constant sourcing of active ingredient of appropriate quality and will safeguard the public.
4.	**What are the categories of product under the scope of API control?**	a) New chemical entity (NCE). b) Prescription, scheduled poison. c) Non prescription, non scheduled poison. **It is only applicable for the **new product registration** application.*
5.	**What is the category of product that does not fall under the scope of API control?**	The following categories of product are excluded from API control: • Traditional product, • Veterinary product • Health supplement product, • Biological and biotechnology product.
6.	**When is the implementation of the API control?**	The implementation will begin with voluntary submission for New Chemical Entities in March 2011 and followed by;

		• Phase 1- New Chemical Entity (mandatory in Jan 2012); • Phase 2- Scheduled Poison, (to be determined); • Phase 3- Non-scheduled Poison (to be determined).
7.	**If products intended solely for exportation purposes, are they required to submit DMF or CEP for API application?**	API used in product for export only (FEO) is exempted from submitting the DMF or CEP in product application.
8.	**What is the procedure for API application?**	Separate registration of the API is not a requirement for the purpose of product registration. However, the required technical documentation pertaining to each API should be submitted with the online product registration application.
9.	**How much is the processing fee?**	Not required as the API application is already incorporated in the product registration application.
10.	**What is the timeline for API application?**	The timeline will be the same as the time taken for product registration.
11.	**What are the required information/documents need to submit for API application?**	a) Certificates of suitability (CEP) or, b) Drug Master File (DMF); c) Current Good Manufacturing Practices (GMP) certificate or any other evidence of GMP compliance from regulatory authority. d) Certificate of Analysis (COA).
12.	**Who should submit the documents?**	The MAH of the product registration shall submit Part 2.S ACTD as part of online product application. Where any information required as per ACTD is not available the DMF will be required. While the API manufacturer shall submit the complete (open part and closed part) of the DMF.
13.	**What are the documentary requirements for a DMF**	From the MAH: Open part of the DMF *from the MAH*, as part of the submitted product dossier (the open part contains most of the information in Part 2.S (ACTD) -

		i.e. sections S1, S2.1 and S3 to S7); S1 General Information 1.1 Nomenclature 1.2 Structure 1.3 General Properties S2 Manufacture 2.1 Manufacture(s)/Site of Manufacture S3 Characterisation 3.1 Elucidation of Structure and other Characteristics 3.2 Impurities S4 Control of API/Drug Substance 4.1 Specification 4.2 Analytical Procedures 4.3 Validation of Analytical Procedures 4.4 Batch Analysis 4.5 Justification of Specification S5 Reference Standards or Materials S6 Container Closure System S7 Stability From the API Manufacturer: The complete (open part and closed part) DMF from the API manufacturer. The closed part contains the confidential information in section Part 2.S.2. ACTD- i.e. section 2); S2 Manufacture 2.1 Manufacture(s)/Site of Manufacture 2.2 Description of Manufacturing Process and Process Controls 2.3 Control of Materials 2.4 Controls of Critical Steps and intermediates

		2.5 Process Validation and/or Evaluation 2.6 Manufacturing Process Development.
14.	**What is the maximum file size acceptable for uploading into the online module?**	Currently, Quest 3 only accepts any kind of documentation format with maximum size 5MB.
15.	**How do I submit the DMF to the NPCB?**	The API Manufacturer may submit the DMF via electronic copy (CD) or hardcopy (optional) directly to the NPCB to maintain confidentiality of the contents within 7 days after the online submission received (payment confirmed). The information contained in the restricted part of the DMF will be regarded as confidential and will only be evaluated in support of the applications mentioned in the Letter of Access. The confidential information will not be disclosed to any third party without a written authorization from the API Manufacturer.
16.	**What security procedure is NPCB putting in place for the submitted CDs, DVDs or Hardcopy of DMF?**	The CDs, DVDs or Hardcopy of DMF will be stored in a secured environment.
17.	**What are the GMP requirements for the API manufacturer?**	Current GMP certificate or any other evidence of GMP compliance from a regulatory authority (as deemed appropriate).
18.	**Does the API manufacturer need to be inspected?**	Depending on the outcome of the evaluation of the API dossier, a risk-based approach will be used in the planning of inspections; the approach will take into account the type of APIs as well as the outcome, results and reports of inspections conducted by other regulatory authorities or competent organisations.
19.	**Does the NPCB accept CEP issued by the EDQM?**	Yes, the NPCB will accept a CEP issued by EDQM in replacement of the DMF of the API.
20.	**How many source of API allowed for each new finished product**	Only two sources of API are allowed.

	application?	
21.	**What is the information need to be submitted if finish product contains more than one API?**	If drug product contains more than one API, the information for each API must be provided.
22.	**Does the applicant need to send sample of the API to the NPCB?**	Currently, NPCB did not ask for the submission of sample of the API for the purpose of registration. However the sample may be required during Post Market Surveillance activity.