EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Work instructions

Title: Calculation of fees for GMP and product related inspections		
Applies to: P-CI-MQC staff		
Status: **PUBLIC**		Document no.: WIN/INSP/2043
Lead Author	Approver	Effective Date: 13-APR-12
Name: Piotr Krauze	Name: David Cockburn	Review Date: 13-APR-15
Signature: On file	Signature: On file	Supersedes: n/a
Date: 04-APR-12	Date: 04-APR-12	TrackWise record no.: 3374

1. Changes since last revision

New WIN.

2. Records

Electronic records of the fees calculated in accordance with this WIN are entered in the Corporate GXP database (Letters to Inspectorates generated by the database are the core records).

A further entry is made in the Inspections tracking sheet (Document Ref. ID: EMA/INS/GMP/840870/2009).

3. Instructions

EXPLANATORY NOTES	
MAH **(Marketing Authorisation Holder)**	For the purpose of this document this term shall include applicants for and Holders of Marketing Authorisations and Plasma Master Files (PMF) or Vaccine Antigen Master Files (VAMF).
Product A, B, C	A product is distinguished by its EMA-number; this distinction applies also to duplicate applications or other co-marketing scenarios.
Manufacturing site / blood establishment	A physical location which contains one or more manufacturing facilities at the same address; whereby a manufacturing facility comprises a separate building or complex of buildings in which a manufacturing activity or activities are carried out. In analogy this

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

EXPLANATORY NOTES	
	applies to Blood Establishments (BE).
Blood Establishment (BE) activities	One or a series of operations related to the manufacture of a plasma pool (e.g. collection, separation, testing, storage, distribution, transport, look-back).
Main blood establishment (BE)	Site chosen amongst the sites to be inspected, usually one performing most of the operations (BE activities).
API activity group	Includes any number of activities related to the manufacture of chemical and biological APIs (active pharmaceutical ingredients); e.g. MCB/WCB (master cell banks/working cell banks), API intermediate, API, QC-API (quality control of the active pharmaceutical ingredient), storage; it does not include the sterilisation of APIs; it applies to VAMF applications.
FP activity group 1 **Sterile Dosage Forms**	Includes any number of activities related to the manufacture of the finished product (FP); e.g. intermediate, bulk FP, primary packaging, secondary packaging, storage/distribution/importation, QC-FP (quality control of the finished product), QC-stability, diluent, adjuvant, excipient and sterilisation of diluent/adjuvant/excipient/ API; it applies to **STERILE dosage forms** such as: +Large volume liquids +Small volume liquids +Lyophilisates +Solids and implants +Semi-solids
FP activity group 2 **Non-Sterile Dosage Forms**	Includes any number of activities related to the manufacture of the finished product (FP); e.g. intermediate, bulk FP, primary packaging, secondary packaging, storage/distribution/importation, QC-FP, QC-stability, diluent, adjuvant, excipient; it applies to the following **NON-STERILE dosage forms**: +Capsules, hard shell +Pressurised preparations +Capsules, soft shell +Radionuclide generators +Chewing gums +Semi-Solids +Impregnated matrices +Suppositories +Liquids for external use +Tablets +Liquids for internal use +Transdermal patches +Medicinal gases +Intraruminal devices +Other solid dosage forms +Veterinary premixes +Other non-sterile medicinal product
Consecutive inspection *(for PMF only)*	An inspection performed in conjunction with an inspection of a main blood establishment (BE) requiring a full fee. Requirements: • Duration no more than 1 day on site. • Linked to the same PMF (dossier) as the main BE. • Carried out by the same inspection team during the same inspection tour.

EXPLANATORY NOTES	
Fee calculation *(general rules)*	• The fee is calculated in the following order: site, product, manufacturing activity. • Fees should be charged separately for each marketing authorisation and calculated separately for each activity group applicable. • The fee regulation does not foresee grouping for the purpose of sharing the fees, i.e. fees are paid per Marketing Authorisation (MA). • Fees should be charged separately for every PMF-application and calculated separately for every inspection tour requested by the CHMP (Committee for Medicinal Products for Human Use) or the CVMP (Committee for Medicinal Products for Veterinary Use) . • Fee calculation for a Vaccine Antigen Master File (VAMF) should be done in analogy to the calculation for biological APIs.
GMP-Co	GMP Inspection Coordinator.

This WIN applies to inspections requested in-line with procedures SOP/INSP/2019 (GMP), SOP/INSP/2009 (PMF) and SOP/INSP/2012 (VAMF).

General provisions for inspection fee calculations can be found in the *"Rules for the implementation of Council Regulation (EC) No 297/95 on fees payable to the European Medicines Agency and other measures"*: EMA external website > Home > Regulatory > Human medicines> Fees.

Detailed explanations and examples on GMP inspection calculation can be found in the *"Explanatory note on fees payable to the European Medicines Agency*" (Document Reference: EMA/283580/2011): EMA external website > Home > Regulatory > Human Medicines > Fees.

For GMP inspections proceed as follows:

Step	Action	Responsibility
1.	Identify the site to be inspected.	GMP-Co
2.	Identify all products linked to this site.	GMP-Co
3.	For each product identify the applicable activity group(s) (i.e. FP activity group 1, FP activity group 2, API group).	GMP-Co
4.	Allocate 1 full fee to each identified activity group for each product.	GMP-Co
5.	Enter the number of fees allocated per product in the Inspections tracking sheet (Document Ref. ID: EMA/INS/GMP/840870/2009).	GMP-Co

Example:

GMP Inspection								
Site	*"Manufacturing facilities at the same address"*							
Product	A		B	C	D	E		
Activity Group	API	FP 2	FP 1	FP 1	FP 2	API	FP 1	FP 2
FEES per activity group	1	1	1	1	1	1	1	1
Fees per Product (per Marketing Authorisation)	**2**		**1**	**1**	**1**	**3**		

For Plasma Master File (PMF) inspections proceed as follows:

Step	Action	Responsibility
1.	Identify the PMF.	GMP-Co
2.	Identify the main blood establishment to be inspected and allocate a full fee.	GMP-Co
3.	Identify all "other" bood establishments to undergo inspections consecutive to the main blood establishment identified (i.e. during the same inspection tour as the main blood establishment).	GMP-Co
4.	Allocate a half-fee to each "other" blood establishment.	GMP-Co
5.	Enter the number of fees calculated in the Inspections tracking sheet (Document Ref. ID: EMA/INS/GMP/840870/2009) under the main blood establishment.	GMP-Co

Example:

PMF Inspection						
PMF A (PMF Holder X)						
Main BE	**other BEs**					
BE 1	BE 2	BE 3	BE 4	BE 5	BE 6	BE 7
Any BE Activities	Any BE Activities	Any BE Activities	Any BE Activities	Any BE Activities	Any BE Activities	Any BE Activities
1 Fee	**0.5 Fee**	**0.5 Fee**	**0.5 Fee**	**0.5 Fee**	**0.5 Fee**	**0.5 Fee**
	Consecutive inspections					
Total of 4 Fees						