GOOD MANUFACTURING PRACTICE

PRE-INSPECTION COMPLIANCE REPORT AND INTERIM COMPLIANCE REPORT

GUIDELINES FOR COMPLETION AND SUBMISSION

Version 7

May 2018

Revision note:

The compliance report has been updated to require provision of PDE data for each active handled on

site in the compliance report provided prior to the inspection. Sites are also requested to advise of any

molecules that are handled on site that may pose a health hazard to inspectors e.g. hormones,

sensitisers etc.

Background

The Pre-Inspection Compliance Report and Interim Compliance Report forms part of the MHRA risk

based inspection system and is required to be completed by each site holding or named on a UK

manufacturing license, sites holding a Blood Establishment Authorisation, API sites, or non UK sites

that are named on a UK Product License.

Pre-Inspection Compliance Report

The Pre-Inspection Compliance Report will be completed in preparation for a Good Manufacturing

Practice inspection of the site, prompted by the notification letter. Change is regarded as either an

indicator of an increase or decrease in risk or as a risk itself. As such the inspector will consider the

changes in planning for the inspection and reaching a conclusion as to the current risk rating of the site.

It should be noted that risk rating is not concluded until after the inspection.

Interim Compliance Report

An Interim Compliance Report should be submitted by sites between inspections following significant

change or as requested by the inspector. This is supplied using the Interim Compliance Report and

provides a report to the inspector of actual changes that occur between inspection cycles. Inspectors

assess the significance of changes reported and may move the planned inspection period based on the

risk presented by the changes. The risk rating will only be changed after a subsequent inspection.

Introduction

The following information is provided for general guidance for completion of the Pre-Inspection

Compliance Report and Interim Compliance.

It is the responsibility of the site to judge what information/data indicates significant change (increase or

decrease) in site risk to GMP Compliance, product quality and patient safety. As individual sites are

best placed to know what changes could have an impact on the above attributes the decision on what

to report is with the site.

This will be reviewed with the inspector during the inspection, it is expected that there may be 'grey

areas' where sites believe changes are not significant but inspectors believe they are or may be

significant. Such cases will be discussed during inspection when sites may be requested to justify their

position. It is the intention of the MHRA to ensure that the Risk Based Inspection system is applied in

an objective manner to allow balanced risk assessments across all applicable sites. Risk rating will be

utilised to define future inspection frequency and duration.

Specific

Guidance

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MHRA are seeking to identify significant changes in a site that would potentially alter, or indicate a

change to, the inherent risk to product quality and patient safety for site activities. In order to complete

this report sites should consider but not limit to the areas recorded below, where no further detail is

given, these questions are self-explanatory. Sites may wish to consider what is reported through

change control, management review meetings or other strategic business meetings and considered

significant by the site:

Shift in performance

1

Please specify markets/territories supplied from each manufacturing unit on the site, with

output figures for each unit per year since last inspection (all global markets).

2 Does the site operate a common Quality system regardless of product destination?

3 Has the company identified any Pharmaceutical Quality System trends or significant

changes? Deviations / complaints / recalls *(if yes provide details)*

Significant changes in numbers of deviations, complaints, recalls or non-conformance identified that indicates a step change in performance of the site or a particular unit or product within the site.

4 Has there been any slippage or amendment to actions agreed with an Inspector to correct

deficiencies from a previous inspection?

Outstanding or overdue Corrective and Preventive Action (CAPA) – major trend changes in

CAPA to be reported rather than individual CAPA i.e. where the ability of the site to close

CAPA within own targets is compromised by continual and repeated examples of failure to hit

due dates or repeated rescheduling of due dates of significant CAPA items.

5 Other Performance Changes to report:

Key

Personne

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l or Staff Numbers

1 Have there been any key organisational changes that would not be picked up through the

manufacturing licensing process e.g. change of site manager (senior person on site) where

this individual is not named on the license? Non UK sites should also report changes in key

QA or Production personnel.

2 Has there been any significant change in total personnel numbers (permanent and/or

temporary) and have there been any announced personnel redundancies or termination of

long term or embedded contract personnel?

(i.e. indicating downsizing of the operation).

Significant addition of staff to meet an upturn in demand should be reported particularly

where this equates to around a 10% increase or more and particularly where temporary staff

will be used to fill the shortfall.

3 Other Key Personnel or Personnel Numbers Changes to report:

Company Ownership/ Structure or Status

1 Has there been any Change of ownership of the site or change of position or role of the site

in the wider organisation e.g. site sale or company merger or takeover, organisation

restructured and site or QA lead reporting through different group or person?

2 Has the site/company entered into administration or is it experiencing financial difficulty that

has/will result in budget cuts affecting good manufacturing practice compliance?

3 Other Company Ownership/ Structure or Status Changes to report:

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Processes/ Products

1 Have there been any changes in the types or numbers of products manufactured / handled.

This should include re-introduction of a product after a period in excess of one year without

manufacture and any products subject to shortages in supply.

Although changes to types of products would be picked up through the licensing process it

may be that a site has re-introduced a product type after a lengthy period without

manufacture. Increase in demand for products may have resulted in increased volumes –

this is particularly significant where shift patterns are changed to accommodate or staff are

recruited, transferred or made redundant.

2 Please populate the table for all actives handled on site - regardless of market or commercial

status (this can be attached as a separate table)

Active

PDE

(µg/day)

Facility

/

Building

Manufacturing

area (s)

Filling

line (if

different)

Primary

Packing

line

Dedicated (√)

Facility Equipment

Please advise if the site handles any product types that would potentially be a hazard to

specific individual inspectors e.g. beta-lactams, hormones etc.

The table can be taken out of the report format and appended to it if this is easier to prepare

outside of the report.

PDE values should be determined via a Health Based Exposure Limit (HBEL) determination

by a toxicologist. If HBEL assessments have not yet been completed, please report the

Active but enter 'not determined' or ND against PDE.

3 Have there been any outsourcing activities or bringing back in-house previously outsourced

activities directly related to production or Quality Control?

4 Have any GMP compliance issues been identified with any API sources that would lead to

the conclusion that the source was not or may not be GMP compliant e.g. critical or

numerous major findings in an audit of the API site, recurring failures on incoming goods

testing of the API?

5 Have there been any Sterility test failures since the last inspection?

If so, please specify the date and product details

6 Has there been any Media fill failures resulting in re-validation in accordance with guidelines

in annex 1of the EU GMP Guide?

If so, Please give date, process/line detail and indication of products affected.

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7 Have there been any significant changes in the number of rejected batches? Please provide

the number since last inspection and details.

The number is to be provided even if no significant number changes

8 For sites operating under a regional or global corporate structure: please list any centralised

functions located at this site (e.g. artwork generation, supplier management, IT support etc)

Please list even if performing on behalf of one sister site

9 Other Processes/ Products Changes to report:

Facilities/Equipment

1 Have there been any changes to facilities e.g. addition or change of use of buildings, major

refurbishments to buildings or utilities, or problems with any of these, that may affect product

quality or the ability to manufacture/supply?

2 Has there been any new or modified equipment used for storage, control, processing e.g.

addition of equipment that introduces new technology to the site?

3 Do you use contract laboratories or sterilisation sites? *(for non-UK sites only)*

If so, please complete the table entering all organisations / sites used.

Name of organisation Address Activity performed

4 Please provide numbers of all out of specification testing results, per year, since the last

inspection (report phase I & II investigation numbers separately). Microbiology and chemistry

OOS numbers should be provided in separate lists.

5 Other Facilities/Equipment Changes to report:

Data Integrity

1 Do you have a policy on data integrity/ governance? Yes / No (no need to supply)

This is simply a YES/NO answer

2 Please confirm that computerised system owners and personnel with administrator-level

access will be made available for the duration of the inspection. Note: if a corporate or global

function performs this then a communication channel with remote access and visibility to all

systems will be sufficient.

This is simply stating an expectation that the subject matter experts for these systems will be

available during the inspection

A YES/NO answer is required.

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3 Has there been any new or modified IT or computerised systems used for storage, control,

processing e.g. Addition of computerised systems such as a new LIMS or manufacturing

execution systems or major modifications to such systems?

This is a YES/ NO – where yes, the system name and date of installation or modification is

required.

4 Please complete the listing of principal computerised systems (e.g. ERP, LIMS,

chromatography systems, eBMR, MES, access control) in the table below as follows. Please

highlight any stand-alone systems.

Please note if the Site Master File contains all the requested details, then please state this

here and provide.

This table may be sent as an attachment if it is easier for the user. Please note; the request

is for principal computerised systems only, this does not include items such as individual

departmental spreadsheets

Type Area Name of

product &

Supplier

Version or

model

Last

qualification

date

Any

modifications/

updates/

patches

Software All

Hardware laboratory

Other changes, quality or compliance issues to be notified.

Any other changes or issues that the site believe may indicate a step change in the sites risk to

product quality or of being non GMP compliant, producing defective batches or affecting patient

safety.

Section 3 Anticipated Changes

Please advise any changes that are anticipated to happen within a period up to two years. It is

expected that these may not be confirmed changes and that information reported will be the best

available at the time. A confirmation of actual changes should be submitted on an Interim Compliance

Report to the inspector once these are definite.

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Specific Guidance for API sites

In order to complete this report sites should consider but not limit to the areas recorded below. Sites

may wish to consider what is reported through change control, management review meetings or other

strategic business meetings and considered significant by the site:

- API or Drug Product recall triggered in any market as a result of issues with the manufactured

APIs named on the GMP certificate or other APIs manufactured on site under the same quality

system.

- API site/company entered into financial administration (or equivalent financial status) or

experiencing a financial difficulty that has/will result in budget cuts affecting good manufacturing

practice compliance.

- Changes in the types of products manufactured/ handled in facilities that manufacture API/API

Intermediates for EU Markets. Particularly introduction of hazardous contaminants to site such

as non pharmaceutical molecules, Ectoparasiticides, highly sensitising materials, biological

preparations containing living organisms, certain hormones, cytotoxics, other highly

active/potent products e.g. teratogens.

- Addition of new manufacturing buildings within the current facility for manufacture of products

named on the GMP certificate.

- Any other significant changes or issues that the site believes may indicate a step change in the

risk to product quality or affecting patient safety.

Mitigating Action

It is the intention to take into account mitigating action taken by sites in relation to change. As such

relevant mitigating action already taken against changes reported should be recorded in a succinct

manner. Evidence of this may be reviewed during the inspection.

Interim Compliance Report - Changes Made Post Inspection

Significant changes confirmed between inspection visits must be reported to MHRA **but only for sites**

that have been inspected post 01 April 09.

The guidance given above for content of the Pre-Inspection Compliance Report should also be

applied to the Interim Compliance Report.

The completed form should be sent by e mail to the inspector that last inspected your site with a copy

to gmpinspectorate@mhra.gov.uk.

For planned changes these should be advised at implementation of the change or if appropriate e.g.

staff redundancies, once the change is confirmed and prior to actual implementation.

These will be assessed by the relevant inspector and impact on the next planned inspection period

assessed. It is intended that risk rating will only be amended following subsequent inspection; sites will

not be formally advised of any change in their next inspection date although this may be informally

communicated by the inspector.

Failure to submit a required Interim Compliance notification of change may be assessed by the

inspector as an increased risk factor.