

Invitation to offer for NHS Generic Pharmaceuticals Wave 10b

Offer reference number: CM/PHG/15/5465

Period of framework agreement: Dates detailed below with options to extend up to a maximum period of 48 months

Potential periods of call-offs under the framework agreement:

100% products:	All regions:	01/11/2016 to 28/02/2019 (28 months)
33% products:	DCE & DSW:	01/11/2016 to 30/06/2018 (20 months)
Housekeeping:	DLS & DNE:	01/11/2016 to 30/06/2017 (8 months)
	DLN & DNW:	01/11/2016 to 30/06/2017 (8 months)

Guidance for Performing a Pharmaceutical Quality Assessment of Licensed Medicines for the NHS

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Introduction

The purpose of the risk assessment process is to support the process for contract procurement of licensed medicines by ensuring that all medicines placed on contract are fit for purpose. The aim of the process is to identify and document any quality issues or risk factors relating to the medicine and its packaging that may give rise to an increased risk of a medication error or patient harm. The assessment forms a critical part of the overall procurement risk management process.

There are two components to the risk assessment:

- Pharmaceutical Quality Assessment (PQA)
- Assessment and evaluation of supporting technical data and identification of potential issues that may cause local implementation problems following a contract change – Potential Acceptability Issues (PAI).

Pharmaceutical Quality Assessment (PQA)

This assessment is aimed at ensuring the medicine meets the technical specification and is of appropriate quality. The assessment also incorporates medication error potential analysis (MEPA). This element of the assessment process is designed to identify the areas of risk associated with the medicines' labelling and packaging, including user information e.g. Patient information leaflets (PIL) and technical data.

The risk assessment is designed to evaluate individual medicines, corporate livery issues (e.g. drug, form and strength differentiation) and livery differentiation issues between different suppliers/manufacturers. The assessment will also include a review of any user feedback issues associated with a product previously on contract.

Potential Acceptability Issues (PAI)

During the assessment, the assessor may identify important information or issues that may be of use to end users. These issues may not pose a medication error risk or highlight a product quality issue, but need to be identified as they may cause local logistical problems or could assist the adjudication process. These should be classified as Potential Acceptability Issues (PAI) and typically include significant changes from the medicine previously on contract that require local impact analysis prior to going on contract. Examples include changes that may require additional work to be carried out by manufacturing units, e.g. stability data, formulation changes; patient acceptability issues (e.g. taste); and differences in licence indications.

The Pharmaceutical Quality Assessment Process

There are a number of potential hazards associated with medicines and their packaging, which can be exacerbated following a change of supplier or packaging, leading to medication errors. These hazards include:

- Confusing one medicine with another due to poor labelling or packaging
- Confusing one medicine with another due to similarity of the manufacturers packaging across its product range
- Confusing a medicine with another after it has been removed from its outer packaging
- Unknowingly using a medicine outside its licensed indications
- Providing the incorrect dose due to complex manipulation or calculations before administration
- Health and safety risks to staff/patients due to poor packaging and labelling
- Impaired quality due to changes in medicine formulation and stability
- Patient acceptability problems related to changes in medicine formulation
- Medicine pack/formulation failing to meet local needs e.g. robot compatibility.

The pharmaceutical quality assessment process is aimed at identifying and assessing any risk factors associated with a medicine under tender. The technical specification (see Document No.05) provides a comprehensive list of criteria to which medicine suppliers should comply and compliance is against this specification is assessed using this assessment tool.

NB the technical specification also contains a section relating to dose form specific requirements which identifies additional issues to the generic quality assessment tool. This should also be referred to where appropriate to evaluate compliance with the tender specification.

The pharmaceutical quality assessment is split into ten sections:

- Critical information
- User information
- Pack design
- Corporate livery
- Dose administration
- Technical data
- Product quality
- Licensing
- Supplier performance
- Robot compatibility

Each section in the pharmaceutical quality assessment (PQA) tool is split into two criteria; essential and desirable (NB every risk component will not necessarily be relevant to the medicine under adjudication).

Any deficiency identified in the assessment should be documented as a risk factor, together with the associated hazard in the PQA comments section of the PharmaQC database.

Any deficiency against the essential criteria will result in at least a medium PQA risk rating. Cumulative risk factors should be evaluated by the QA specialist and a high PQA risk rating allocated where appropriate.

Individual deficiencies in the desirable criteria should be documented in the PharmaQC database to allow feedback to the supplier, but should be allocated a low PQA risk rating.

Multiple failings in the desirable criteria may lead to a medium PQA risk rating at the discretion of the QA specialist if the risk factors are deemed to be cumulative.

Where relevant, a digital photograph should be taken to highlight any deficiencies or issues raised at the assessment and this should be uploaded onto the PharmaQC database.

Any additional points of concern or information that may cause problems with local implementation should be documented in the PharmaQC database as a PAI to allow the adjudication teams to review the issue and assess its impact.

Assigning PQA Ratings

High Risk - There is a significant quality issue and risk to patient safety, the product should not be placed on contract unless there is no alternative and that effective risk reduction measures are identified and implemented.

If any single risk category is deemed to be a critical risk, the product is automatically assigned a high overall PQA risk rating.

Medium Risk - There is an overall low/medium risk to patient safety, but there are medium/major risk factors associated with the medicine. Risk reduction measures should be identified and implemented where possible. This should include dialogue with the company to resolve the issue and intermediate control measures such as the issue of safety action bulletins. (If there is a product from another manufacturer with a low risk, then that product should be placed on contract).

Low Risk - no major risks identified, safe to go on contract without any corrective course of action.

Assessing Artwork Only

Occasionally, samples are not available for assessment and the supplier will forward artwork only for pre-assessment. In this case the assessor should carry out the PQA assessment for the artwork only and identify any deficiencies as for a normal sample.

When entering the results of artwork-only assessments onto PharmaQC, the assessment should be allocated an artwork only rating, which identifies the assessment as being incomplete at the time of adjudication to the adjudication team (The artwork only symbol can be selected from the drip down box for PQA risk ratings). All risk factors should be reported in the PQA comments section as below (reporting of results), together with comments relating to the limitations of the artwork only assessment (e.g. Artwork satisfactory – Low PQA risk rating for artwork).

The assessment should then be completed on receipt of the sample and the artwork only symbol replaced with the overall PQA risk rating.

Reporting of Results

The results from the risk assessment for each product assessed are entered into PharmaQC. This should include the overall risk assessment rating (PQA rating), any associated comments and an uploaded digital image which clearly demonstrates the deficiency (where appropriate). The comments should clearly state the potential hazard and the associated risk factors and be written to facilitate both feedback to suppliers and to allow direct data export into safety medication bulletins without the need for further editing.

Suggested Actions for Medium/High Risk Rated Products

- Award the contract to a safer alternative where possible. This decision is made and documented by the adjudication team
- Identify any risk reduction measures e.g. issue safety medication bulletin or “caution in use”. Risk reduction measures are identified by both QA specialists and adjudication teams. The safety medication bulletin is produced by QCNW on behalf of the NHS QA Committee
- Advise end users to perform a local risk assessment on the product – advice disseminated locally by lead representatives of regional/divisional purchasing groups
- Change local practice if necessary (e.g. storage in different locations, ward briefings etc) - advice disseminated locally by lead representatives of regional/divisional purchasing groups
- Monitor effectiveness of risk management measures using local error reporting mechanisms - review of quality issues by QA specialist from AIC database and NHS CMU summary report
- Inform Industry, regulatory body (MHRA), contracting & purchasing authority and National Patient Safety Agency when necessary – carried out by QA specialists on behalf of NHS QA Committee procurement sub group.

Pharmaceutical Quality Assessment (PQA) Tool

General

The product under assessment must match the product description under tender.

NB When assessing modified or slow release preparations, ensure they meet the exact description under tender.

1. Critical information

Critical information is defined as:

- The generic name of the medicine
- The strength of the medicine
- The form of the medicine
- The route of administration
- Posology
- Warnings

Essential criteria

- All critical information must be present (this includes small containers such as ampoules and vials)
- The name of the medicine expressed on the packaging should be the same as registered in the summary of product characteristics (SPC). NB this will be the brand name for a proprietary product, but the generic name should also be clearly expressed. No Abbreviations
- If the medicine contains more than one active ingredient, all generic names should be clearly stated on the pack. 'Co-' names should be as registered on the SPC and labelled as part of the name
- Strengths should be clearly expressed and unambiguous. For injections, the strength should be expressed both as total quantity per total volume and as amount per unit dose (e.g. milligrams per ml) where appropriate. Trailing zeros should not be used. Microgram doses should be spelt out rather than abbreviated. (**NB** pay special attention to different strengths/concentrations across injection product ranges)
- Base and salt strengths should be clearly defined where appropriate.

Desirable Criteria

- The brand name should not be similar to another generic or brand name in either appearance or sound.

2. User Information

Essential criteria

- Only positive statements should be used on labels for routes of administration e.g. 'For intravenous use only'. Negative statements such as 'not for intrathecal use' should not be used
- All patient packs should include a patient information leaflet (PIL).

NB The assessment process does not require a review of the content and design of the PIL, as this is reviewed by the licensing authority. The following two sections are for reference only.

- The PIL should provide the following key information:
 - What the medicine is used for
 - Any precautions prior to taking the medicine (allergies, contraindications, drug interactions, pregnancy and breast feeding guidance, driving/operating machinery etc.)
 - How to take the medicine
 - Possible side effects
 - Storage requirements
 - Information relating to other ingredients
 - Product description
 - Company details - Name and address of MA holder and manufacturer.
- The design and layout of the PIL should allow the patient to easily find and understand the important messages within the leaflet. This should include:
 - An index to allow easy navigation
 - Consistent headings that stand out using larger font or bold text
 - Colour should only be used judiciously to allow good contrast of key messages
 - Good readability - text should adequately spaced and as large as possible. (dense text can lead to loss of concentration)
 - The use of complex language and medical jargon should be avoided. Information should be translated into lay language
 - Side effects should be grouped by seriousness and should give clear guidance as to when to take action, and what the action should be
 - Related information should be located together
 - Repetition should be avoided.

3. Pack Design

Essential criteria

- The critical information should be given due prominence and located together in the same field of view where practicable (i.e. these items should not be broken up by additional information, logos, background texts or graphics)

- When the name of the medicine is a Brand name, the generic name of the active ingredient should preferably be given prominence, but as a minimum standard be clear, easy to read and be in the same field of view as the critical information. There should be no intervening text
- The generic name and strength should appear on at least three non-opposing sides of pack (including “shelf” end)
- The marketing authorisation and name and address of the licence holder should be present on the pack
- The batch number and expiry date should be present and legible, particularly when embossing is used rather than print. The expiry date should be unambiguously expressed (e.g. “use before” or if using “expires”, the full date of expiry should be expressed in day/month/year)
- Temperature storage conditions should be clearly stated on both the primary and secondary packaging
- Products that are sensitive to light should be labelled with “protect from light”. For these products, the primary packaging should be designed to protect the product from light (not just the secondary packaging), especially when the product is commonly removed from the secondary packaging and stored locally (e.g. vials in aseptic units and infusions in clinical areas).

Desirable Criteria

- When relevant, colour should only be used judiciously to aid identification of critical information (consider innovative designs)
- The name & strength of the medicine should be printed legibly over each blister or oriented repeatedly across strip
- Ampoules should be labelled longitudinally
- Patient packs should have a space for placement of the dispensing label. This should be a blank white space in which there is no text, to aid legibility of the dispensing label. Where it is not possible to employ a blank space, the pack should be of a colour that will not interfere with the readability of the dispensing label.

4. Corporate Livery

Essential criteria

- There should be good differentiation between different medicines within the corporate livery of the company. Consideration should be given to similar or look-alike names (INN and Brand) and potential problems associated with storage due to alphabetical location
- There should be good differentiation between strengths within the product range

- There should be good differentiation between different formulations of the same product intended for different parenteral routes (e.g. intravenous and intrathecal).

Desirable Criteria

- There should be good differentiation between dosage forms within product range.

NB when assessing a single line, assessors should refer to other images on PharmaQC to assess corporate livery criteria.

5. Dose Administration

Essential criteria

- Instructions for dosage manipulation should be clear and unambiguous (consideration should be given as to who will be administering the medicine)
- If complicated calculations are required to calculate the dose (e.g. dilutions, conversions from milligrams to millimols, mg/kg dosing in children etc.), unambiguous instructions, conversion tables and/or labelling should be provided
- If specific end user counselling is required, clear patient instructions should be provided to aid this process (e.g. inhalation devices used in asthma treatment)
- If additional devices are required to administer a dose, this should be supplied with the medicine along with clear instructions for its use.

Desirable Criteria

- Medicines should be in a ready to administer dosage form whenever possible. Solutions should be provided in preference to powders for reconstitution where formulation allows. If reconstitution or serial dilution is required, instructions must be prominent, clear and unambiguous
- The SPC or specific user guidance should be included in the packaging for medicines requiring further manipulation by health professionals (e.g. fluid compatibility and infusion rates for injections).

6. Technical Data

Essential criteria

- Displacement values should be provided for any injection requiring reconstitution
- Diluent compatibility data should be provided for any injectable dosage form that requires dilution or reconstitution prior to infusion
- The recommended diluent should be clearly stated in the SPC and/or packaging
- The shelf life and specified storage conditions following opening or reconstitution should be clearly stated in the SPC and on the packaging.

Desirable Criteria

- Stability and compatibility data should be available for injectable medicines commonly prepared as infusions in aseptic units. All data should be comparable to the brand leader and should include:
 - Physico-chemical compatibility with common diluents (sodium chloride 0.9% , glucose 5 % etc)
 - Physico-chemical compatibility with common containers + packaging (polypropylene, glass, PVC etc)
 - Route of chemical degradation
 - Physico-chemical compatibility with other drugs
 - Degradation rate
 - Shelf life at 4°C and 25°C in recommended diluents
 - Validation for use with common reconstitution devices.

7. Product Quality

Essential criteria

- Tablets and capsules should be marked for easy identification or be visually distinctive
- Scored tablets should be easily halve
- There should be no evidence of damage or lack of dose uniformity in tablets
- Pack closures should be tamper evident
- Patient packs should have child resistant closures
- Powders intended for dissolution should dissolve easily
- Suspensions and emulsions should re-suspend easily upon shaking
- Labels on vials/ampoules intended for use in aseptic units should be resistant to spraying and wiping with alcohol
- Containers containing cytotoxic medicines should be clearly labelled with a suitable warning on both primary and secondary packaging
- Primary packaging of medicines commonly used in aseptic units should be easy to disinfect and not provide “dust traps” e.g. some fracture resistant containers
- Oral liquid medicines should be sugar free and alcohol free when specified in the description. NB non-cariogenic sugars that are suitable for diabetics are acceptable in sugar free formulations (e.g. liquid maltitol)
- Details of any excipients in the formulation should be provided (name and strength)
- Labelling of eye preparations should be as clear as possible to facilitate use by visually impaired patients.

Desirable Criteria

- Tablets /capsules in blister packs should be easily 'popped out' and the blister pack should have no sharp edges
- Tablets and capsules should be packed in blisters or patient packs to prevent unnecessary handling
- The taste of liquid formulations should be acceptable for all patient groups
- Vials and oral liquid formulations intended for reconstitution must be of sufficient size to allow reconstitution in accordance with its SPC and with the volume of diluent commonly used in aseptic units (not just to allow bolus administration at ward level)
- Cytotoxic products should be presented in fracture resistant containers
- Vials should be compatible with commonly used reconstitution and docking devices where appropriate.

8. Licensing**Essential criteria**

- The medicine must be licensed for use in the UK
- The licensed routes of administration should be clear and obvious
- The licensed indications and routes of administration should be comparable to the brand leader where appropriate. (NB this should only be assessed for transition tender products. Results should be raised as a PAI rather than as a PQA score. This element of the assessment is carried out by Medical Information and is outside the scope for the PQA assessor).

Desirable Criteria

- None.

9. Manufacturer Performance

An awareness of company performance issues relating to medicine quality is taken into account during the assessment. Points of reference may include the following:

- Recalls associated with the medicines or company
- Minor defects reported for the medicine or company
- Quality issues reported to CMU
- MHRA liaison meetings
- Supplier audits taken on behalf of the NHS
- User feedback issues identified on the PharmaQC database.

Specific issues should be raised as either a PQA or PAI comment as appropriate when deemed relevant by the PQA assessor.

10. Robot Compatibility

Essential criteria

- The pack should be compatible with automated dispensing systems. (NB this element is assessed by CMU)
- A bar code should be present on the pack.