GUIDANCE ON MANAGING THE SOURCING AND SUPPLY OF READY-TO-ADMINISTER CHEMOTHERAPY DOSES FOR THE NHS

A 'How to' Guide

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INTRODUCTION

Target Audience and Scope

This document is aimed at staff in UK NHS hospitals considering or already sourcing their supply of chemotherapy as ready-to-administer doses. This could be:

- As fixed dose syringes and infusion bags to support dose banding (see below) either out sourced from a third party or in-sourced via batch produced chemotherapy dose banded products from their own licensed aseptic unit
- As Individualised patient specific doses from either from other NHS units or from non NHS commercial organisations (both of which must hold a Manufacturer's Specials (MS) licence from the Medicines and Healthcare products Regulatory Agency (MHRA))

Many of the risks highlighted will apply in all of these situations, so the majority of hospitals should find this document useful. The principles may apply to other types of aseptic products.

Sourcing refers to obtaining supply of ready-to-administer chemotherapy doses rather than in house patient specific aseptic preparation.

For the purposes of this document the term chemotherapy applies to all parenteral Systemic Anti-Cancer Therapies (SACT), including traditional cytotoxic chemotherapy, monoclonal antibodies, immunotherapy and targeted agents.

Regional/National Procurement Arrangements

The consideration within this document apply to products are sourced both internally by hospitals and for those that have been awarded on national/regional contracts. Readers are advised to seek clarification from Regional procurement specialist on what risk mitigation measures that will have been included in national/regional procurement, e.g. supplier approval.

What is Dose Banding?

Dose banding is a system whereby drug doses which are calculated are grouped and rounded to a set of pre-defined doses. Each series of consecutive dose(s) is called a 'band', with the dose to which they are rounded towards being the 'banded dose'. A single national dose banding system has been in place in hospitals in NHS Scotland for a number of years. In April 2016 NHS England launched a National dose-banded system with standardised doses (1). The aim was to ensure the same dose banding system is used throughout England. Dose banding is an enabler of outsourcing, however it is possible to outsource chemotherapy supply without dose banding and it is possible to dose band without outsourcing.

From 2016, hospitals in England have been encouraged, via a NHS England Commissioning for Quality and Innovation (CQUIN) incentive schemes, to standardise chemotherapy dosing using the new dose banding national system. Many hospitals already utilise dose banding and outsource supply of ready-to-administer dose-banded products. Once prescribing by the same dose bands has been established nationally, there should be opportunity for greater efficiency in preparation or procurement of dose-banded products over time.

Sourcing And Supply of Ready-To-Administer Chemotherapy Doses

Chemotherapy dose standardisation, through dose banding, supports the National Medicines Optimisation agenda in England.

As prescribing by dose banding becomes established and, following Carter (2), the Hospital Pharmacy Transformation Programme (HPTP) gets underway, hospital aseptic services will be reviewing their capacity and looking at the potential for making supply of chemotherapy dose-banded products more efficient.

This document discusses the practicalities of implementing a system of sourcing and supply of standardised doses of chemotherapy, whether in-house or outsourced. It gives guidance on both understanding the risks in the outsourcing and supply process and on ways of ensuring that the necessary control measures are in place to minimise these risks.

While it is possible to apply dose standardisation to any chemotherapy product, it will rarely be possible to batch produce all chemotherapy doses and so any model for supply using batch produced doses will still require either an in-house arrangement or external supplier for supply of single doses, for example of short shelf life products.

SECTION ONE: PRACTICAL CONSIDERATIONS

Key Responsibilities

Any decision to outsource the supply of chemotherapy products should be agreed by a hospital governance committee with responsibility for chemotherapy and/ or medicines, e.g. Medicines Management Committee, Drug and Therapeutics Committee. It is advisable for NHS England Specialised Commissioners to be involved in discussions with the hospital on the financial implications of outsourcing chemotherapy. Note these products are unlicensed medicines.

The appropriate hospital committee should document their understanding that ready-to-administer chemotherapy are unlicensed medicines and ensure compliance with organisations policy. It must then be highlighted to all NHS staff involved in the prescribing, receipt and dispensing of ready-to-administer chemotherapy that these are unlicensed products and, as such, this places particular responsibilities on the staff involved. (Individual doses prepared in-house with expiry periods beyond those in the manufacturer's Summary of Product Characteristics are also classed as unlicensed.)

The Chief Pharmacist has overall responsibility for medicines management within an NHS organisation. In practice this means that they are ultimately responsible for ensuring that effective governance arrangements are in place across the organisation for all injectable medicines, whether prepared in pharmacy or outsourced (3). If a decision is made to outsource chemotherapy products, the Chief Pharmacist therefore has the final responsibility to ensure that the appropriate approvals and Quality Assurance checks are in place, in the same way as they would be required to for doses prepared in-house.

For outsourced products, it is essential that the responsibilities of both the contract giver (purchaser) and contract acceptor (manufacturer) are clearly defined and formally agreed by each party in line with EU GMP (4). Service level and technical (quality) agreements, detailing the key aspects of the service, responsibilities and Key Performance Indicators (KPIs), need to be in place. These need to be more than standard template documents, and must consider specific local circumstances and needs. Realistic expectations of service provision must be agreed between both parties and responsibilities for quality must be defined in the technical (quality) agreement (TA). Agreements will need to be monitored to be effective. The hospital (the contract giver) needs to ensure adequate staff resource, both in terms of time and seniority, is available to monitor agreements.

Where the product prescribed could be supplied using a product prepared in line with the product licence but the pharmacy considers that it is more appropriate to supply a product with an extended shelf life, the share of any burden of liability is likely to be increased towards the pharmacist rather than the prescriber, especially where any harm resulting relates to product quality rather than the clinical selection of the drug.

The NHS Pharmaceutical Quality Assurance Committee guidance document entitled

‘Guidance for the Purchase and Supply of Unlicensed Medicinal Products – Notes for Prescribers and Pharmacists’ states (*5).* ‘A practitioner prescribing an unlicensed product or for an unlicensed indication, does so on his/her own responsibility. Consequently, he/she carries the burden of the patient’s welfare and in the event of adverse reactions he/she may be called upon to justify his/her actions.

A pharmacist will share responsibility:

1. As the purchaser of the product, particularly where this involves specifying the product to be purchased;

2. If his/her actions or omissions have contributed to the harm.'

In light of point 1 above, NHS hospital pharmacists (acting as the purchaser) must be particularly aware of their responsibility for specifying a suitable product and not be reliant on the manufacturer (contract acceptor) ensuring this is the case. As such, pharmacists undertaking this role must have a suitable level of training in, and knowledge of, the formulation and stability of chemotherapy products. They will also need to ensure they have sufficient knowledge of how the product will be used clinically, or have worked with clinical pharmacy colleagues to ensure these considerations have been taken into account. Quality Assurance measures should be in line with the receiving organisation's (contract giver's) unlicensed medicines policy.

The manufacturer (contract acceptor) will be responsible for any breaches of Good Manufacturing Practice, but they cannot take responsibility for the clinical suitability of the chemotherapy products purchased, unless providing a clinical pharmacy service is part of their contract (which is outside the scope of this guidance).

The NHS Pharmaceutical Quality Assurance Committee's document 'Quality Assessment of Unlicensed Medicines' (6) gives specific advice on the quality assessment of aseptic 'Specials' and should help hospitals discharge their responsibilities for monitoring product quality and, hence, protecting patient safety.

Managing Capacity for Chemotherapy Supply

It should be noted that outsourcing of chemotherapy, which can be beneficial in reducing the workload of pharmacy aseptic units, may have an impact on the cost per item of products made in local hospital aseptic units as the number of doses made internally will fall whilst overheads remain fixed. Ideally a balance is needed, with the NHS maintaining aseptic unit capacity to prepare chemotherapy whilst taking advantage of commercially-prepared dose-banded products that will save capacity in aseptic units, and should reduce waste and provide financial benefits.

It should also be remembered that often the workload associated with the ordering, checking and dispensing of outsourced products, and monitoring the technical agreement (TA) and Service Level Agreement (SLA) (see below), is not inconsiderable and must also be taken into account in capacity calculations.

Investment in outsourcing, where appropriate, will be more cost effective in the first instance than investing in new aseptic facilities, and should therefore be carefully considered. NHS commissioners of chemotherapy services in England are of the view that dose banding, either in-house or from an external provider, should be implemented to manage chemotherapy capacity.

There is potential for hospitals to work together to centralise aseptic production across multiple NHS sites. This is in line with current NHS thinking (2). In this scenario, the hospital(s) without aseptic units will need to follow the advice in this guidance and treat their NHS supplier as an external provider, unless both hospitals are within the same legal organisational boundary.

The NHS supplier will need to hold a Manufacture Specials licence (MS) from the MHRA, and the supply of chemotherapy must take place under that MS. Note, it is possible for a hospital to supply chemotherapy to another NHS hospital without an MS if they are registered with the GPhC, and have sight of the original prescription (7).

Hospitals must assure themselves that any supplier realistically has the capacity to provide the volume of products that they will be using. However, they must also ensure that they provide accurate and realistic data to the supplier about the volume and length of supply likely to be needed. At the time of writing there is a lack of capacity in both NHS and non-NHS units to meet rapidly increasing demand.

Supplier Approval

A key aspect of supplier approval is audit. The actions below may have been undertaken as part of regional procurement process. Hospitals should nerveless assure themselves that the questions below have been considered in discussion with their local/regional procurement or QA specialist.

A supplier audit will give a valuable independent insight into actual activities at a supplier's site however is only a "snapshot" on the day of the audit. Reliance will often be placed on an audit conducted by a third party. Obtaining a copy of an audit report, whilst important, is only the start of the process. There needs to be a formal consideration of the audit report with regards to specific local circumstances of the hospital. This should consider:

- Did the auditor have suitable knowledge and experience?
- When was the audit performed, and is it still relevant?
- What was the scope of the audit?
- Is this relevant to the proposed outsourcing? (An audit of non-cytotoxic manufacture may not be directly relevant to chemotherapy, for example. Likewise, an audit of patient-specific chemotherapy supply may not be applicable to batch supply.)
- What was the outcome of the audit and what recommendations were made?
- What was the supplier's response to the recommendations and was this appropriate and timely?

It is also appropriate to ask to see the most recent MHRA audit report and the action plan to address deficiencies identified. Other quality information e.g. GMP certification, copies of MHRA licences, etc. should also be requested and reviewed. Check that the supplier has the relevant product types covered under their licence. Following assessment of information regarding quality of supplier, there should be a formal sign off of approval (if appropriate) by the person in the organisation with responsibility for pharmaceutical product quality.

Technical (Quality) Agreements

To capture all the detail above, a formal Technical Agreement must be in place between the NHS purchaser and any external manufacturer. This needs to be a meaningful, live document that describes how the outsourcing arrangements and associated responsibilities of each party will be managed. It must not simply be seen as a regulatory requirement.

The technical agreement (TA) should be drawn up, agreed and signed by someone performing a quality role in both the NHS organisation giving the contract (this could be part of the role of, for example, someone with a medicines safety remit, aseptic services pharmacist etc.) and the provider of the service. It should define, in practical terms, the responsibilities of both parties with regards to the safety and quality aspects of the products provided. The TA therefore should have been agreed by those with responsibilities for those aspects of the service rather than for sales / contracting.

The TA could either be a two-party agreement between hospital and supplier (see appendix B for example) or in instances where regional contracting is undertaken, a three-party agreement may be preferred to clearly define the responsibilities of all parties. Check with local/regional procurement and QA specialists for preferred TA template.

Hospitals must be assured that their chosen supplier will not further subcontract work without an agreed written authorisation being received from them. This should be formalised in the TA.

A formal contract or a Service Level Agreement (SLA) will also be needed, defining the arrangements for the provision of a timely, cost effective and efficient service. This should be signed by both parties by a senior person in a procurement role, in line with the contract giver's standing financial instructions.

A template for a TA for chemotherapy, based on one included in the 5th Edition of the Quality Assurance of Aseptic Preparation Services: Standards Part B support resources, forms Appendix B of this document and may be a useful guide to the type of content required.

Contracting and Ordering

Hospitals who are considering outsourcing are advised to contact the leading manufacturers of dose-banded products and undertake a budget impact assessment of commercially-supplied dose-banded products.

Efficiency may be possible by working collaboratively with other hospitals and/ or as part of a regional process. Consideration will need to be given to tendering process and complying with procurement regulations. As this is a competitive commercial area, use of NHS Specialist Pharmacy Services (SPS) including pharmacist contracting and quality assurance expertise is strongly recommended, e.g. the local or regional specialist purchasing pharmacist(s).

Quality and sustainability of supply are as important considerations as unit price. The supplier with the cheapest commercial price may not necessarily be the preferred supplier. Therefore, hospitals should also involve quality assurance colleagues to support them in the outsourcing process.

Sourcing And Supply of Ready-To-Administer Chemotherapy Doses

A decision to outsource chemotherapy supply, which will have an impact on budgets, will need discussion with relevant commissioners of services, including Health Boards (in Scotland and Wales) and NHS England Specialised Commissioning Teams (in England) as well as local hospital finance teams.

Outsourcing may be seen as beneficial by commissioners where an on-cost is paid to hospitals to prepare ready-to-administer doses. It should be noted, however, that it is not the commissioners who are taking the responsibility for the quality of these unlicensed medicines – it is the purchasing organisations if the products are outsourced (as they would be if prepared in-house).

Hospitals should discuss with commissioners how the costs of supplying outsourced chemotherapy (including the costs of dispensing an individual dose and the costs of managing the supply chain) are to be met, especially where a switch in supply route will result in a reduction in other income for the hospital.

Within England, the Payment by Results Guidance (8) states that: *"The costs of each of the* [chemotherapy] *procurement HRGs contain all costs associated with procuring each drug cycle, including supportive drugs and pharmacy costs (indirect and overheads)."* However many hospitals have alternative arrangements in place to reimburse the pharmacy costs for chemotherapy and the impact of switching to ready-to-administer doses will need to be discussed with NHS England.

Order lead times should be considered to ensure that the manufacturer has adequate time to process, manufacture and release the products in a timely and safe manner, while also ensuring that the hospital will not need to hold excessive stock levels resulting in waste**.** This should be covered in the SLA/TA. If separate organisations work in partnership, they will require a Wholesale Dealers Authorisation (WDA) to transfer stock between sites. Responsibilities should be clearly defined in a 3-way technical agreement (manufacturer and both NHS organisations)

Contingency Plans

Hospitals must have in place contingency plans for continued supply of essential chemotherapy medicines for patients should outsourced suppliers be unable to meet demand.

Suppliers also need to have in place contingency plans to ensure continuation of agreed supplies. Contingency plans need to consider how the service will cope with increasing demand, and reduced capacity for example due to staff illness, planned down-time, natural disaster, fire, terrorism, etc. These considerations should account for the supplier's staff and facilities and infrastructure connecting the supplier to the purchasing authority.

The contract acceptor must notify the purchaser before any contingency arrangement is implemented. The product supplied under any such arrangement must be identical to that supplied by the main contractor unless otherwise agreed. This should specifically be in the TA.

Hospitals must assure themselves that their chosen supplier’s plan is realistic and actionable. It is appropriate to ask the supplier for evidence of the effectiveness of the plan to minimise risk to patients.

Complaints and Key Performance Indicators (KPIs)

Formal systems with agreed, named contacts are needed for communication between the hospital and the manufacturer regarding complaints associated with products and/or services. (The KPIs may have been agreed as part of a regional procurement process.)

The process for dealing with complaints and suitable timelines should be agreed and responsibilities defined in the TA. Hospitals need to be assured that robust systems are in place to provide timely feedback on subsequent investigations and corrective and/ or preventative actions.

Responsibilities in relation to recalls should also be clearly defined in the TA. This needs to include recalls on active medicines, but also diluents and other components used during the manufacture of the product such as syringes. Timescales for responses to recalls should be agreed in the TA. Suppliers should be able to provide assurance that they have sufficient infrastructure in place to communicate with all their customers in a timely manner, including confirmation to the purchaser of receipt of the recall.

A meaningful set of KPIs must be agreed by both the purchaser and supplier and these should be continually monitored and discussed at a formal review meeting at least annually.

Purchasers should, however, have on-going programmes of monitoring trends in KPIs and a formal mechanism should be agreed for raising any significant concerns.

In addition to service related items, e.g. turnaround times, KPIs should include some quality indicators such as out-of-specification results, complaints etc. It is recommended that NHS organisations work together to define a minimum data set for KPIs for outsourced products.

SECTION THREE: LOGISTICAL CONSIDERATIONS

Delivery from Suppliers

Hospitals need to be aware of the logistical arrangements for the delivery of outsourced chemotherapy to their site(s) and agree with the manufacturers that these arrangements are appropriate and will give a high degree of assurance that the products have not been adversely affected during transport. Deliveries need to be made according to GDP (Good Distribution Practice)(9). Evidence to demonstrate compliance with this requirement should be able to be provided by the manufacturer. The requirement for this should be included in the TA.

Issues to be considered include:

- Ensuring the ordering systems used by purchaser and supplier are fit for purpose.
- What are likely transit times?
- How will packaging be marked? Will pharmacy stores staff be aware of its hazardous nature? Will they be aware of special storage requirements?
- Will packaging be resistant to leaks?
- What delivery contractors will be used? How likely are deliveries to be affected by adverse weather such as snow and flooding?
- Segregation, e.g. separate boxes if receiving intrathecal products and avoidance of mixed products loose in a box
- How orders are packed and shipped by supplier to aid receipt/unpacking by storekeepers in the receiving hospital
- Clarity of labelling of outer packaging of multiple items

Cold/Ambient Chain considerations:

- Is refrigerated transport or a time-limited cold chain transfer box to be used?
- For refrigerated transport, are delivery-specific data available and will notification of excursions be given? Hospitals need to consider if that notification is likely to result in a request to quarantine stock if this may adversely impact patient care depending on the expected time between receipt of a drug and issue to a patient.
- For cold chain transfer boxes how, and for what period, have they been validated, and did this reflect realistic worst case scenarios? Is there on-going monitoring or revalidation of specific deliveries? Note: cold chain considerations also apply for distribution within the organisation.
- Could ambient temperature storage products, be exposed to cold or excessive heat in transit?
- Clear identification of storage requirements (to reduce risk refrigerated items being left at room temp or vice versa)

Consideration should be given to arrangements in place for the receipt of deliveries out of hours, if appropriate.

Hospitals must also ensure they understand the impact of Bank Holidays and planned service down-time on ordering lead times. Hospitals need to plan for lead times being affected not only by production schedules being changed but also by increased demand for service from other customers.

Logistics within Hospitals

Hospitals receiving pre-filled syringes/ infusion bags for the purpose of dose banding must complete accountability records in line with local policy for the receipt and dispensing of products and ensure good practice for handling unlicensed medicines, in line with the organisation's unlicensed medicines policy. Factors to consider include:

- Ensuring involvement of Quality Assurance (QA) advice on processes.
- The need for increased fridge space for storage of stocks of ready-to-administer products. This needs to include consideration of storage for stock, goods in quarantine, goods pending dispensing checks and outbound goods which may be dispensed further in advance than would traditionally have happened. In addition, number of times fridge(s) are accessed will increase so the fridge(s) should be sufficiently robust to cope with this increased activity.
- Storage space should take into account the hazardous nature of the product and the need to minimise the risk of syringes being dropped. It is important to ensure that, in the event of a spillage, any risks to staff from exposure are minimised.
- The range of syringe sizes chosen to ensure that all dose bands can be delivered without using an excessive number of syringes. As a guide, it should usually be possible to develop a syringe inventory that requires no more than one extra syringe to administer a dose than the minimum number required to supply the dose had the same maximum syringe filling rules been applied.
- The need to specify labelling requirements, light protective packaging, fill volume limits and closure type for syringes, with the manufacturer and to ensure these are compatible with existing hospital practices. (See appendix A, point 18)
- The cold chain integrity within the hospital (as there must be evidence that the cold chain had been maintained if unused doses are to be recycled.) There will need to be a robust system to identify any stock being returned for destruction (for instance due to adverse storage) from anything being returned for re-use.
- There will need to be an area suitable for dispensing of syringes to individual patients. As this may include removing outer packaging to apply dispensing labels to inner containers, consideration will need to be given to the potential for environmental challenge as the outer packaging would normally provide a degree of protection from microbiological contamination. There is no need to undertake this activity in a clean room, but the area should be of suitable size and degree of cleanliness. In addition, packaging provides containment for spillages and so consideration of the health and safety risks will need to be given. Gloves should certainly be worn when handling the inner packaging and may be advisable when handling outer packing.
- If the outer wrap has been removed, after risk assessment of the process, the inner container should be suitably re-packaged to reduce risk of microbiological contamination and to contain any spillage. This may require access to a heat-sealing machine. While this may be shared with an in-house preparation facility, thought needs to be given to the impact of any increased footfall to access equipment in controlled environments.

- The positioning of labels on inner products and outer packaging must not obscure critical information on the manufacturer's label. Likewise, any light protective packaging needs to be carefully thought through to ensure inner labels can be checked easily.
- There will need to be adequate segregation of stock from dispensed items, with consideration of storage for items pending checks.

Some hospitals may prefer to establish arrangements where patient specific ready-to-administer doses are supplied directly to the clinic or ward. Such arrangements must be clearly described in the TA and/or SLA including the prescription pathway, clinical checks and release by a pharmacist. The Chief Pharmacist of the purchasing hospital will remain responsible for ensuring the quality of the medicines supplied and compliance with relevant legislation, e.g. concerning unlicensed medicines. As doses must be labelled for individual patients Information Governance considerations will apply since patient identifiable data will need to be shared with third parties.

Risk assessment of products that are not patient specific, e.g. bags for stock, must be undertaken as part of consideration of supply directly to the clinic or ward.

Much of the same considerations above will still need to be considered regarding cold chain of products, including systems for handling returns. Furthermore, thought will need to be given to how suppliers will check they are dispensing the correct dose to the correct patient if they are unable to access the patient's prescription. Any transcription to an ordering system will inevitably carry a degree of risk and should be carefully investigated during audit.

Where deliveries take place directly, rather than through the pharmacy, e.g. homecare, the pharmacy should consider what system should be in place to selectively have oversight of the product being supplied including, for instance, labelling and compliance with specifications. Assurance of compliance with product specification should be part of the routine contract management.

Ordering Systems

It is important that those involved in the procurement of ready-to–administer medicines understand how their order will be handled by the supplier. Consideration should be given to minimising the risks of transcriptions both within the hospital prior to transmission to the supplier/manufacturer and transcriptions at the supplier which may result in incorrect goods being sent.

The use of facsimile for transmission of orders can be prone to error and poor quality of faxes can result in loss or addition of unwanted decimal places very easily. Electronic data interchange (EDI) ordering is possible with some suppliers; however, other suppliers will require more detail on orders than can easily be included on EDI orders, such as intended routes of administration. Patient-specific information cannot usually be included on EDI orders. Many suppliers now offer ordering directly via their own websites, however it should be noted that these may not interface with the hospital system. EDI may reduce transcription risks and delays at the supplier end, but this should not always be assumed to be the case. If orders are to contain patient-identifiable data, advice from Information Governance will need to be sought.

Hospitals should understand what validation process takes place after receipt of an order with the supplier.

Failed deliveries due to, for example, manufacturing delays, lost orders and problems with the road network, can cause unexpected pressures for the hospital which can have an impact on capacity and adversely affect patient experience. Hospitals, during the contracting process, should seek to identify how suppliers will communicate any delays to them. On-line order tracking can be very beneficial, especially where hospitals are working on a 'just-in-time' model for deliveries.

SECTION THREE: QUALITY CONSIDERATIONS

Ideally the actions in this section should be undertaken centrally on behalf of the NHS as part of a regional procurement process. Hospitals taking part in such a process must assure themselves that these actions have been completed and are applicable to their particular situation.

Stability and Shelf Life

Hospitals should not simply accept shelf lives as offered by the supplier/manufacturer but need to have an understanding of on what data this shelf life is based. Chemotherapy stability can be a complex issue that inevitably requires a degree of interpretation of available data for each specific drug. This is particularly true for biopharmaceuticals. Hospitals should have an insight into the source and quality of the data being used as a basis for the shelf life decision, and should assure themselves that it specifically applies to their products. For example, is the concentration the same as in any published studies? Is the container the same?

Consideration needs to be given to potentially harmful degradation products as well as active chemical components and microbiological stability. In addition, stability testing, particularly for biological molecules, needs to consider the impact of transportation. Microbiological integrity testing should also consider transportation and should refer, for example, to the specific syringe and blind hub combination in use. (10,11)

Hospital pharmacy teams need to have a sufficient level of knowledge of stability to allow them to make an informed decision as to the robustness of the shelf life being offered by their supplier. If there is insufficient expertise in-house, they should consult other NHS colleagues who do have this level of knowledge or consider developing in-house expertise.

Assessment must look at the robustness of the data underpinning the allocated shelf life, not just the relative length of the shelf life as compared to other manufacturers.

Risk of Composition Errors and Microbiological Contamination

Any chemotherapy products that are aseptically prepared are subject to risk of microbiological contamination and composition errors. While the nature of cytotoxic chemotherapy can suppress some bacterial growth, the effect is not consistent across all cytotoxic compounds or pathogens (12).. Furthermore, no bacteriostatic effect would be expected with most biological medicines. In addition, the patient population treated with chemotherapy is generally immunosuppressed, placing them at an increased risk of infection if contamination is present. Therefore, while the risk of growth during storage may be less than for example, parenteral nutrition, precautions against microbiological contamination both during preparation and storage are still needed. Where a manufacturer provides a product labelled for storage between 2 to 25°C, storage should normally be under refrigerated conditions.

Staff responsible for any outsourcing process need to have an understanding of both these types of risks, including knowledge of the production process used by their chosen manufacturer, and what controls and tests are incorporated into their processes to manage these risks.

The TA should require the manufacturer to inform the hospital of microbiological out-of-specification results that could potentially impact on the quality of their products. Suitable arrangements should be in place within the purchasing organisation to knowledgeably assess the significance of this information. Final responsibility to use or not use a product will still rest with the pharmacy even if the manufacturer deems there is not cause to recall it.

Chemical, Microbiological and Sterility Testing

Purchasers must be aware of the type and frequency of process validations undertaken and be assured that these, combined with other control measures and testing, offer a satisfactory level of assurance of the aseptic process.

Hospitals must involve their local pharmaceutical Quality Assurance expert(s) to support them in assuring that the supplier's processes for chemical, microbiological and sterility testing offer adequate level of assurance in the quality of the products supplied.

Purchasers must agree and specify with the manufacturer the level of testing of the processes to assure quality of the products supplied. This should be documented in the TA.

Purchasers must be aware of each manufacturer's capability with regards to the chemical, microbiological and sterility testing of manufactured cytotoxic syringes and bags, including the type of process used to produce them.

As well as considering the sterility testing programme in place, hospitals should be aware of what end-of-session and operator validation schedules the manufacturer is using and be satisfied that these provide a sufficient level of sterility assurance for their products.

Traditional sterility testing requires incubation for 14 days and so results are, for the most part, retrospective and give historical assurance data for the process only.

Any failures must be reported to the receiving hospital(s) and included in the TA.

New rapid microbiological techniques are being developed and some manufacturers are considering the potential for these to give sterility results before product release. This should be investigated with the manufacturer.

Hospitals must be aware of (or seek appropriate expert advice on) how these technologies are used and that this gives an appropriate level of sterility assurance for the products being purchased.

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12. Peiris V, Oppenhiem BA. Antimicrobial activity of cytotoxic drugs may influence isolation of bacteria and fungi from blood cultures. J Clin Pathol. 1993;46:1124–5.

Appendix A: Checklist for Hospitals Undertaking Outsourcing

To be agreed with suppliers (some steps may be undertaken as part of contracting process)

1. Agree on a range of drugs and doses (ensuring compliance with nationally approved dose bands) and include this in the SLA.

2. Develop a specification for each product required. (It may be possible to accept the existing specification from the manufacturer, but this should be carefully assessed for suitability e.g. labelling, presentation, protection from light).

3. Ensure that the syringe or final bag volume for each dose is also agreed as part of specification, making sure that the volume in a syringe does not exceed the maximum recommended percentage (normally no more than 85% of nominal volume). ***Note*** many chemotherapy drugs given in syringe are done so as slow bolus over several minutes therefore need to consider the ability for nursing staff to safely administer the syringe volume without risk of repetitive strain. Some hospitals may use syringe pumps to assist administration and therefore accept higher syringe fill volumes. Hospitals will need to work with their clinical teams to understand the needs of their end users.

Syringe Size	Maximum Fill Volume
1ml	0.85ml
3ml	2.5ml
5ml	4ml
10ml	8ml
20ml	17ml
30ml	25ml
50ml (60ml nominal size)	50ml (However consider suitability of large volumes for hand pushing)

*syringes should be graduated in ml, not cubic centimetres, and graduations should be appropriate to the volume being measured

4. As part of specification, agree what information will be on any patient specific individualised doses, ensuring it meets needs of clinical areas, complies with hospital medicines and information governance policies.

5. Establish what end-product stability and sterility testing is required and agree the specification, limits and responsibilities as part of the TA

6. Ensure validation of the cold chain supply has been undertaken, including special considerations for seasonal variation and distance to travel, especially if using an overnight delivery.

7. Agree what information will be on the documentation received routinely with the product, in line with the product specification.

8. Establish the capacity limits of manufacturer as part of SLA. Include in the SLA the proviso of notification when maximum capacity is being approached by the manufacturer.

9. Create a contingency supply plan to account for the manufacturer being unable to meet the demand to ensure continuity of chemotherapy provision. (This is to minimise risk to patients' treatments.) This plan could include SLAs with alternative suppliers of chemotherapy (NHS manufacturing units or non NHS suppliers), but needs to acknowledge that other NHS organisations may also be seeking contingency support at the same time.

10. Establish order deadlines, minimum orders etc. and ensure these are adequately shared with relevant staff in pharmacy.

11. Understand the process for placing orders with suppliers and receiving feedback on order handling and expected delivery dates and times.

To be undertaken internally within pharmacy for outsourced dose-banded products

12. Ensure electronic systems are set up to use the agreed products and dose bands

13. Create a standardised order form for banded doses (listing doses and quantities in units) and create procedures for stock management, ordering and for the transcription of orders between systems (e.g. Pharmacy Stock Control System to Supplier Website Ordering System.) Particularly for individual patient specific prescriptions, ensure that there are robust procedures for the creation and checking of orders. Ensure that these procedures are compliant with the hospital's Standing Financial Instructions and Information Governance requirements.

14. Create an SOP(s) for receipt, QA assessment, storage and release of dose-banded products into pharmacy stock and ensure there is sufficient capacity within pharmacy to carry out quality checks of outsourced products prior to, or as part of, the dispensing process.

15. Train staff on the requirements for the receipt, QA assessment and storage of products.

16. Identify an adequate area for the dispensing, labelling and packaging of products being labelled from stock, and for segregation of stock, dispensed items pending checks and outbound goods.

17. Provide adequate information to support product selection by pharmacy staff. For instance a grid of doses with the strengths of syringes needed to be combined to achieve this dose.

18. Create a SOP(s) for dispensing of dose-banded products and/ or patient specific doses and include these as competencies to be met in individual staff training documentation. Consider including guidance on label placement in the SOP and ensure adequate light and microbiological protection will be provided to the dispensed product.

19. Stocks of externally sourced dose-banded products should come pre-labelled with the agreed label (see points 2 and 4 above). Pharmacy departments dispensing dose-banded products will need to label the product with a minimum of patient name, patient identifier, e.g. hospital or NHS number and date issued. Ideally, this label will be on the outer wrap as well as the product, unless the product label is clearly visible through the outer wrap.

20. Prepare an SOP for labelling and dispensing of dose-banded products from stock. Risk assess the process for breaching the outer packaging from a COSHH and microbiological contamination perspective versus not labelling primary container with patient details.

21. Update any existing pharmacy procedures describing the processes to be followed in the event of a Drug Alert / Product Recall/Devices Alert to ensure that the impact on products supplied through third parties is adequately considered. Test the SOPs to ensure that the accountability process is sufficiently robust to be able to identify any doses at any stage of the supply chain through to patient level.

To be undertaken internally across the chemotherapy service

22. Establish prescription receipt deadlines for patient specific individualised doses.

23. Set deadlines for routine delivery of product(s), incorporating dispensing time and distribution from the pharmacy to the clinical areas.

24. Establish out-of-hours contacts in case they are needed.

25. Agree with nursing teams where information is duplicated across both the manufacturer's label and the pharmacy label and which version should be used during clinical checks.

26. Establish a documented process for handling of returned products to ensure an adequate cold chain is maintained and that segregation of any products for destruction is suitable.

Appendix B: EXAMPLE OF QUALITY TECHNICAL AGREEMENT

FOR THE MANUFACTURE AND DELIVERY OF READY-TO-ADMINISTER CHEMOTHERAPY DOSES

This is a two-party TA template agreement, between Hospital and Supplier. In instances where regional contracting is undertaken, a three-party agreement may be preferred.

Check with local/regional procurement and QA specialists for preferred TA template.

Between

Name of NHS Organisation (Contract Giver – CG)

And

Name of Supplier (Contract Acceptor – CA)

Validity: This agreement is valid for [*insert suitable timeframe*] after the date of the final signature or earlier if requested by either party

Version:
Reference:

QUALITY TECHNICAL AGREEMENT
For the Manufacture and Delivery of Ready-to-Administer Chemotherapy Doses

This Technical Agreement is made between:

Name and Address if NHS Organisation (CG)

and

Name and Address of Supplier (CA)

Production Unit Site Address:
MS number:

This contract is supplemental to any financial agreements and any subsequent agreements, between the two parties and will last for the duration of the agreement. The technical agreement shall be reviewed every [*insert suitable timeframe*] or earlier if requested by either party.

This Technical Agreement is executed in duplicate, all of which shall be deemed to be originals, and all of which shall constitute one and the same Agreement binding upon both parties.

This Quality Technical Agreement shall be effective as of the date of the final signature and shall remain in effect until review or termination.

1. Scope

This agreement defines the roles and responsibilities between CG and CA relating to the manufacture and delivery of ready-to-administer chemotherapy doses for patients under the care of CG.

All parties agree as follows:-

2. Subject of the Agreement

1. CA is a provider of ready-to-administer chemotherapy doses which are manufactured according to an agreed specification and delivered to CG.
2. CA shall manufacture and deliver the products in accordance with this technical agreement and in addition to other financial agreements.
3. CA is subject to registration and inspection by the competent national authorities and holds the necessary manufacturing licence according to the respective legislation.

CA hereby acknowledges that CG is relying on the skill and experience of the CA in the proper manufacture and delivery of the contractual products under this Agreement and the CA accordingly warrants to CG that:

- The product shall be of satisfactory quality and fit for purpose.
- The product shall comply in all respects with the order provided by CG

Both parties will strictly observe the detailed pharmaceutical responsibilities which are specified in Appendix 1 (“Responsibilities”).

CG and CA must appoint the Contact Persons, as named in Appendix 2 (“Contact Persons”).

3. Regulatory Information

CA is responsible for ensuring that the manufacture and distribution of products meets all current legislation and best practice guidelines.

For the period of the contract CG will ensure that they hold suitable MHRA approval for the supply of ready-to-administer chemotherapy doses.

4. Starting Materials

CA shall source starting materials which possess a UK marketing authorisation. Materials must be sourced from a bona fide Manufacturer or Wholesaler holding a UK Wholesale Dealer's Authorisation.

In the event of unavailability of a licensed starting material, the CA should notify the CG for approval before use of an unlicensed alternative.

5. Manufacture

CA shall provide adequate premises, equipment and staff to satisfactorily carry out the work undertaken. CA shall perform all operations in accordance with Good Manufacturing Practice.

CA shall manufacture the doses in accordance with the specification provided by CG.
CA shall refrain from performing any activities that could adversely affect the quality of the service provided

6. Quality Control / Assurance

CA must provide sterility assurance of all products purchased by CG. The method to determine sterility assurance must be in line with current Pharmacopoeial requirements and be compliant with current guidance e.g. MHRA Q&As.

CA shall obtain satisfactory stability information for each ready-to-administer chemotherapy dose before allocation of an expiry date. This data shall be provided to CG upon request.

Release of each batch of product shall be under the authority of an authorised releasing officer.

CA shall maintain a suitable Pharmaceutical Quality System.

CA acknowledges that CG will perform sample inspection on doses received. Any deficiencies found during the sample inspection which relates in some way to the product supplied by CA will be notified back to CA at the earliest opportunity. This may lead to a formal complaint.

CA shall provide Certificates of Conformance for each batch supplied. The Certificate of Conformance shall at a minimum specify:

a. Name and site of manufacture
b. Name or description of product
c. Product Batch or Lot number
d. Batch size
e. Storage conditions
f. Expiry date
g. Date of manufacture

h. Statement that the product has been manufactured in compliance to applicable GMP requirements
i. Name, title and signature of person responsible for the validity of the certificate and the data it contains.

7. Storage and Distribution

CA shall adhere to Good Distribution Practice.

CA shall ensure that product shall be delivered in accordance with agreed procedures and records of delivery and receipt shall be retained by each party to affect a satisfactory audit trail in the event of recall.

CA shall store, handle and distribute the product according to its defined storage conditions.

CA shall be required to provide evidence that the appropriate storage temperatures have been maintained and that all systems have been validated upon request.

CA shall ensure all products are packaged in such a way as to give them adequate protection from damage during transit.

8. Documentation

CA shall archive completed documentation according to current regulatory guidance.

9. Change Control

Information related to any planned change to the product, overall process or specification for the product(s) by CA is to be notified to CG in writing at the earliest opportunity and authorised by CG prior to the change being effected.

It is recognised that problems relating to the supply of starting materials may require urgent action. The substitution of any starting material with an equivalent material that holds a UK marketing authorisation should be notified to CG at the earliest opportunity, prior to implementation. The substitution with an unlicensed material, if supply issues dictate, should be specifically approved with the CG before implementation..

In the event of merger, acquisition or facility closure of CA or any of its agreed subcontractors, CA shall notify CG at least three months before the change is implemented.

CA shall not delegate or sub-contract any of the work entrusted to it under the Contract Agreement without prior evaluation and approval of the arrangements by CG. Any such arrangements made between CA and any approved third party shall ensure that the information relating to this contract is made available and remains confidential in the same way as between CG and CA.

CA shall be responsible for inherent responsibilities of their sub-contractors. Terms of this TA must be adhered to by any approved subcontractor.

10. Unplanned Deviations

Information relating to any major or critical unplanned deviation associated with the individual product supplied, or overall process, by CA is to be notified to CG in writing at the earliest opportunity e.g. prior to the product being delivered.

Unplanned deviations which do not directly relate to a contractual product but could impact on the quality of a product purchased by CG should also be reported at the earliest opportunity.

11. Complaints

Any complaint from CG concerning the quality of supplied product shall be acknowledged by CA within 24 working hours.

A report containing details of the investigation with corrective and/or preventative actions, as appropriate, shall be forwarded to the CG within ten working days; this may take the form of an interim report if the investigation has not been completed within this timeframe. The CA shall make every effort to complete investigations and provide feedback including actions assigned to CG in a timely manner.

Any complaint regarding non-adherence to this TA by either party should be escalated to the line manager of the relevant signatory for this agreement if a satisfactory outcome cannot be achieved by discussion. Ultimately if a satisfactory outcome still cannot be achieved, financial penalties or termination of the contract may be considered.

12. Recalls and Returns

CA shall notify CG of any recall or near miss (company or MHRA led) relating to contracted products manufactured by CA, or starting materials / components which were used in their manufacture.

Recalls and near misses which do not directly relate to a contractual product but could impact on the quality of a product purchased by CG should also be reported at the earliest opportunity.

The CA shall co-coordinate and document the recall process. The CA is responsible for coordination and disposal of all products returned by CG patients. CA will co-operate with the collection, logging, storage and segregation of any recalled and returned product as required.

13. Audit

CG is responsible for assessing the competence of CA to carry out successfully the work required. This may be through review of a relevant audit performed on behalf of the NHS.

CA shall perform internal audits and perform audits of any outsourced activities.

CG is entitled to audit CA facilities relevant for the manufacture of the contractual products on a bi-annual basis and on specific occasions, e.g. “For-Cause-Audits”. Dates for bi-annual audits shall be mutually agreed at least four weeks in advance, For-Cause-Audits one working day in advance.

14. Confidentiality

The information contained in this agreement is confidential and must not be divulged to any other party without the permission of all signatories.

15. Contingency

CA must ensure a robust contingency plan has been arranged to ensure continuity of service in the event that they cannot provide the pre-defined quantities of ready-to-administer doses as defined by CG. The use of any sub-contractors must be agreed by CG prior to

implementation (see above). Any contingency partner must agree to the terms within this technical agreement.

Final Provision

Amendments of this Quality Technical Agreement and its Appendices may only be carried out by mutual consent and shall be made in writing. Any amendments to the appendices 1-5 may be signed for CG by a responsible Quality representative and together with the signature of CA the appendix will be binding upon the parties.

Appendices

Appendix 1 Responsibilities
Appendix 2 List of Sub-contractors
Appendix 3 Technical Agreement Approval
Appendix 4 Key Contact Persons
Appendix 5 Version History

Appendix 1 Responsibilities

	CG	CA	Comments
1. Regulatory Processes			
Hold appropriate 'specials' manufacturing licence of relevant national authority in order to manufacture products as agreed by CG. Comply with any and all EU and other local current applicable laws, regulations and guidelines relating to GMP and GDP. CG is to be informed of any changes to licence, outcome of regulatory inspection and any pending regulatory action. Actions to remedy any deficiencies identified by regulatory inspection shall be made available to CG upon request.		✓	
Ensure pharmacovigilance systems are in place to collect and collate information concerning all suspected adverse events / reactions reported to CG.	✓	✓	
Report pharmacovigilance events to CA.	✓		
Ensure competent authorities are notified of all complaints concerning suspected adverse events / reactions / lack of effect according to existing regulations and requirements.	✓	✓	

	CG	*CA*	Comments
2. Starting / Raw Materials and Excipients			
Purchase sterile materials with a UK MA from bona fide suppliers.		✓	
Assess the quality of starting materials for use		✓	
Ensure all starting materials are TSE/BSE free		✓	
Maintain a supplier qualification programme.		✓	
Check that the condition of all containers, closures, seals and labelling of delivered starting materials are satisfactory for use.		✓	
Approve of materials for use.		✓	

	CG	CA	Comments
3. Packaging Material			
Only purchase primary packaging materials from approved suppliers in accordance with a specification.		✓	
Maintain a supplier qualification programme.		✓	
Check that the condition of all packaging material is satisfactory for use.		✓	
Approve of packaging for use.		✓	

	CG	*CA*	Comments
4. Processing			
Undertake Qualification / Validation according to applicable GMP requirements for production equipment, utilities and processes.		✓	
Maintain a suitable environment		✓	
Maintain a specific batch number system to identify individual products.		✓	
Manufacturing process, including all necessary activities.		✓	
Ensure In-process checks are performed and are deemed satisfactory.		✓	
Ensure appropriate design and use of manufacturing batch documentation.		✓	
Ensure all critical automated processes are fully validated and appropriate for use and meet the requirements of GAMP.		✓	
Ensure that all products are manufactured in accordance with the agreed specification and current legislation.		✓	
Handle medicines with appropriate safety measures.		✓	
Ensure all labelling of products is in compliance with all laws, regulations and guidelines associated with the labelling of unlicensed specials.		✓	

	CG	CA	Comments
5. Stability			
Provide stability data to support the allocated expiry of the products. (Methods to determine product stability shall be in line with current regulatory requirements.)		✓	This data shall be made available to CG upon request.

	CG	CA	Comments
6. Sterility			
Provide sterility assurance using methods defined in current guidelines.		✓	
Maintain a suitable system to record, investigate and risk assess all microbiological non-conformances (out-of-limit) results. Implement appropriate corrective and/or preventative actions following the investigation and root cause analysis.		✓	
Assess the potential impact a microbiological non-conformance (isolated result or 'trend') could have on product quality and patient risk and act accordingly.		✓	
Trend microbiological non-conformances.		✓	

	CG	CA	Comments
Make available an annual summary of all microbiological non-conformances to CG, on request.		✓	
Inform CG of any microbiological non-conformances relating to products received by CG within 48 hours of receipt		✓	It is recognised that this may be in retrospect. Microbiological non-conformances which do not directly relate to a contractual product but could impact on the quality of a product used by a patient of CG should also be reported. The investigation and any associated corrective and preventative actions shall be made available upon request by CG.

	CG	*CA*	Comments
7. Product release			
Release product according to agreed criteria.		✓	
Prepare of documentation for release.		✓	
Have satisfactory systems in place that ensure patients only receive released products.		✓	
Ensure released product conforms to order placed by CG.		✓	

	CG	*CA*	Comments
8. Storage / Distribution			
Undertake Qualification / Validation of storage sites for starting materials and products as appropriate.		✓	
Undertake Qualification / Validation of transport of the products from place of manufacture to the CG.		✓	
Store all products and/or starting materials / other ingredients / excipients / auxiliary materials under appropriate conditions in compliance with GMP/GDP requirements and any licence requirements.		✓	
Maintain an audit trail to the patient.	✓	✓	
Use delivery containers that ensure the product is protected during delivery and complies with health and safety standards.		✓	
Distribute to the CG in a timely way as described in this technical agreement and other financial agreements.		✓	

	CG	*CA*	**Comments**
9. Documentation			
Ensure that prescription forms as well as records of manufacture and distribution are clear, readily available and retained for the period required by current legislation. Records shall ensure the traceability of the origin and destination of products.		✓	
Ensure that prescription forms/orders are clear and legible.	✓		
Archive documents according to current regulatory guidance.		✓	
Ensure written procedures are available to describe all operations that may affect the quality of the products.		✓	
Maintain complete and accurate records relating to the manufacture, packaging and storage of products supplied.		✓	
Store all documents and records so that they are easily retrievable and stored protected from loss and damage.		✓	
Maintain a record of batch numbers of all starting materials and products manufactured, supplied or returned in the event of a recall.		✓	

	CG	*CA*	**Comments**
10. Changes			
Maintain a suitable change control system and communicate all information relating to planned changes, with quality implications in writing, before implementation.		✓	See above for timelines.
Notification and approval of unlicensed starting materials in the event of non-availability of licensed product.	✓	✓	CA to notify, CG to approve if acceptable.
Maintain a suitable unplanned deviation system and communicate all unplanned changes (unplanned deviation excluding microbiological results) deemed to be major or critical. Events shall be reported at the earliest possible opportunity e.g. before delivery of the product.		✓	Unplanned deviations which do not directly relate to a contractual product but could impact on the quality of a product used by a CG patient should also be reported. The investigation and any associated corrective and/or preventative actions shall be made available upon request by CG.
Results of any investigation relating to a major or critical unplanned deviation for a contracted product shall be provided in written format to CG within 72 hours of completion.		✓	This investigation must include proposed corrective and/or preventative actions.
No work should be sub-contracted without the prior written agreement of CG.		✓	

	CG	*CA*	**Comments**
11. Complaints			
Acknowledge any complaints from CG, or patients of CG, with quality implications within working 24 working hours.		✓	
Investigate and document any complaint relating to the quality of contracted products within 10 days. Feedback may be in the form of an interim or final report. This document should include details of all corrective and/or preventative actions as appropriate.		✓	
12. Recalls			
In the event of product or any starting materials or components being recalled, arrange for the collection, stocking and segregation of products affected. This also includes products which were manufactured using a recalled starting material or component.		✓	Must comply with timelines as specified in regulations
Maintain a product recall procedure for use when it is necessary to recall a defective product from market, and test the procedure at least annually.		✓	This also includes products which were manufactured using a recalled starting material or component.
Advise CG if they have received products which are / contain starting materials which are subject to MHRA Drug Alert or Recall.		✓	Must comply with timelines as specified in regulations
Inform prescribers of any recalls concerning products supplied to patients.	✓		

	CG	*CA*	**Comments**
13. Audit			
Provide reasonable access, at agreed pre-determined times, to permit audits of the relevant facilities and documents by CG or the regulatory authorities.		✓	
Undertake the necessary quality audits of CA	✓		
Undertake the necessary quality audits of subcontractors as required for assurance of this agreement.		✓	
Conduct internal audit in order to monitor the implementation of and compliance with GMP and GDP.		✓	
Propose necessary corrective measures following internal audit.		✓	
Make available evidence of adherence to internal audit schedules.		✓	
Make available evidence of closure of external audits and inspections, and the anticipated date of the next MHRA inspection.		✓	
Conduct inspections of all subcontractors in order to monitor the implementation of and compliance with GMP		✓	

	CG	*CA*	**Comments**
and /or GDP.			

	CG	*CA*	**Comments**
14. Training			
Undertake training of staff involved in all aspects of the service, as appropriate to their role.	✓	✓	This includes training for outsourced contractors
Ensure staff comply with relevant legislation and NHS requirements concerning both patient and commercial confidentiality e.g. Data Protection Act.	✓	✓	

Appendix 2

List of Subcontractors

e.g. Couriers, Contingency partners and Contract Laboratories

Appendix 3

Technical Agreement Approval

Agreed on behalf of the Contract Giver

Name:	Name:
Title: (QA Representative)	Title:
Signature: _____	Signature: _____
Date:_____	Date:_____

Agreed on behalf of the Contract Acceptor

Name:	Name:
Title: (QA Representative)	Title:
Signature: _____	Signature: _____
Date:_____	Date:_____

Appendix 4

Key Contact Persons

Contract Giver

Name	Designation	Contact number	E-mail

Contract Acceptor

Name	Designation	Contact Number	E-mail

Appendix 5

Version History

Version Number	Date of Amendment	Amendment(s) Made