

Toolkit:

How to Implement Dose banding of Chemotherapy

2008

**Andrew Gillian
Network Pharmacist (NELCN)
on behalf of
Cancer Network Pharmacists
Forum**

Acknowledgments

It would not have been possible to create this document without the support and advice of the Cancer Network Pharmacists Forum, NPQAC, NPASG, PASA and the willingness of individual Hospitals involved in dose banding, throughout the UK, to freely share their information and experience.

Contents	Page No
1. Purpose of the toolkit	2
2. What is dose banding?	2
3. Body Surface Area calculations – sources of inaccuracy	3
4. Is Dose Banded Chemotherapy safe and efficacious for patients?	3
5. Benefits of Dose Banding	4
6. Disadvantages of Dose Banding	4
7. When is dose banding not recommended?	5
8. Implementation guide	6
9. Financial and contracting considerations	7
10. The practicalities of dose bands – deciding band structure, using bands to prescribe, dispense and administer chemotherapy	8
11. Frequently Asked Questions	10
12. Areas for future research	11
13. Bibliography	12
Appendix 1. BSA Formulae and other sources of variance.	13
Appendix 2. Factors affecting clinical outcome of chemotherapy.	15
Appendix 3. Examples of banded drugs and regimens and useful contacts.	16
Appendix 4. Sample Business Case.	26
Appendix 5. Guidance for the purchase and supply of unlicensed medicinal products - notes for prescribers and pharmacists. NPQAC. 3 rd Edition June 2004	28

1. Purpose

This toolkit provides guidance to facilitate the introduction of dose banding by hospitals in England and Wales. Scotland has already implemented a National policy on dose banding. The 'evidence' base for dose banding is explored. Examples of good practice and sample dose banding schedules are provided.

2. What is dose banding?

Dose banding has been defined as follows:

'A system whereby, through agreement between prescribers and pharmacists, doses of intravenous cytotoxic drugs calculated on an individualised basis that are within defined ranges, or bands, are rounded up or down to predetermined standard doses. The maximum variation of the adjustment between the standard dose and the doses constituting each band is 5% or less. A range of pre-filled syringes or infusions, manufactured by pharmacy staff or purchased from commercial sources, can be used to administer the standard dose' ⁽¹⁾

Key considerations in the decision to introduce dose banding are:

- (a) Dose banding is a pragmatic approach to dose selection. The selection of a variance limit of +/- 5% is arbitrary – although this limit has been widely accepted by clinicians. Fixed dosing is used for oral chemotherapy which results in a 3 to 5% variance from BSA calculated dose for most patients.
- (b) Sources of inaccuracy and variance in Body Surface Area (BSA) calculations. [\(See Appendix 1\)](#).
- (c) Imprecise relationship between BSA, dose density of chemotherapy delivered to the tumour site and desired therapeutic outcome or levels of toxicity.
- (d) A need to rationalise chemotherapy services in order to meet the growing demand for increasingly complex chemotherapy using finite resources. Use of chemotherapy for cancer treatment is increasing by approximately 10% per year without a similar expansion of staff or facilities.

3. Body Surface Area Calculations – controversies and sources of inaccuracy

3.1 There are inherent inaccuracies in methods of weight and height measurement undertaken in clinical settings. (For example: lack of standardisation, lack of regular maintenance or calibration of weighing scales, variable techniques and equipment employed for height measurement). Variation in body size during the course of disease is not always accounted for.

3.2 The limitations of chemotherapy dosing based upon BSA are outlined in a recent review. ^(2, 3) Some of these are listed below:

- BSA is estimated by formulae, not measured.
- BSA formulae take no account of obesity or cachexia
- BSA does not take account of a large variety of factors relevant to inter-patient variability in drug disposition.
- There is no precise correlation between BSA and drug clearance.
- There is no direct relationship between BSA-based dosing and therapeutic outcome.
- Different BSA formulae give different results. [\(See Appendix 1\)](#)
- The most popular formula, Dubois & Dubois, is based on only 9 subjects. ⁽⁴⁾
- Rounding usually occurs during calculation of BSA and calculation of dose to be given (dose /m²) and again to give a convenient and measurable dose. Some e-prescribing software, such as 'Chemocare' also dose rounds.

4. Is Dose Banded Chemotherapy safe and efficacious for patients?

The key question is whether administering a very large range of individualised, BSA-based doses produces better patient survival rates and less toxicity than the use of standardised banded doses which introduce of up to $\pm 5\%$ variance in dosage. The answer to this question is not known at present. There is some published evidence that fixed dosing is as good as BSA based dosing. Use of oral chemotherapy incurs the same variance ($\pm 5\%$) by using fixed dosing. [\(See Appendix 1\)](#).

Study of the effect of dose banding on treatment outcome is complex and there are no published studies, although at least one study is in progress. ⁽⁵⁾

The outcome of chemotherapy treatment is influenced by a large number of variables such that it is difficult to isolate the contribution of dose-banding alone. (See Appendix 2).

Where dose banding has been adopted into clinical practice this has been based upon the following pragmatic rationale:

Dose banding does not add significantly to the level of imprecision inherent in BSA-based dose calculations nor significantly alter the dose-density of chemotherapy administered over a treatment course.

The quantifiable service and patient benefits achieved by banding outweigh any theoretical disadvantages.

5. Benefits of Dose Banding

More than 48 Hospitals in the UK use dose banding. ^(6, 7, 8, 9) Some introduced the practice as long ago as 1996. Greatest benefit is expected in large busy units. The following benefits have been identified:

- Dose rationalisation
- Fewer dose calculation errors
- Reduction in phonecalls to prescriber or prescription alterations for dose rounding
- Quicker dispensing through use of pre-prepared doses (Pre-filled syringes or infusions)
- Administration of chemotherapy on any chosen day is facilitated
- Reduced patient waiting times
- Adoption of National contract pricing for chemotherapy (Scotland)
- Rationalisation of demand, with aseptic capacity liberated for more complex chemotherapy and more time for clinical duties
- Reduced wastage by re-use of cancelled doses and avoidance of incomplete vial usage during production
- Use of smaller syringe sizes making bolus administration easier
- Easier processing of dose reductions at short notice
- Supports treatment of patients closer to home

6. Disadvantages of Dose Banding

- The administered dose may vary from the BSA calculated dose by up to $\pm 5\%$
- Up to three syringes may be needed for each bolus dose
- Effect of filling, or administering, multiple syringes on incidence of repetitive strain disorder for either aseptic operators or nurses administering chemotherapy has not been researched
- Banded doses *may* be more expensive (acquisition cost) if 'out-sourced' although PASA negotiation can reduce costs.

7. When is Dose Banding not recommended?

Children:

Advice of specialists within Paediatric Oncology and Haematology must be sought if considering dose banding. Dose banding is not prohibited in paediatrics but it is rarely used for a number of reasons. ⁽¹⁵⁾ For example:

- Dosing in children is difficult up to 30kg/8-10 years. UKCCLG recommends a range of dose reductions to BSA calculated doses for children < 12 months old.
- A 10kg child could be a large 9 month old or an underweight 14 month old.
- Relatively small numbers of patients per hospital site
- Most treatment is within clinical trials, banding is not approved in the protocols and methods of drug administration have not been consistent between trials
- Impractically small dose increments may be needed between bands
- Sites preparing batches of dose banded chemotherapy for use in clinical trials may need an IMP manufacturer's license
- Banding across the whole paediatric age range would result in an impractically large number of dose bands

Cachexia and obesity:

Local or Network policy should be followed for dosing in these circumstances to ensure neither over- nor under-dosing occurs in cachexic or obese patients.

Clinical Trials:

Dose banding can only be used in clinical trials with prior agreement of the trial chief investigator and sponsor (preferably discussed during protocol development). With the exception of pharmacokinetic trials, there is no sound reason to exclude dose banding from trials which use BSA based dose regimens, provided effects on dose-limiting toxicities are considered.

Hospital policy:

Each Trust must seek the agreement of clinicians providing oncology and haematology services before introducing dose banding.

8. Implementation guide

8.1 Groundwork

- Identify drugs and regimens for suitable for banding.
- Confirm acceptable shelf-lives for banded products.
- Draw up banding tables. ([See Appendix 3](#))
- Calculate the potential impact of using pre-prepared doses on pharmacy workflow, prescription turn-around times, proportion of chemotherapy dispensed in advance and patient waiting times or day case scheduling (Use C-PORT when available).
- Use and encourage multi-disciplinary collaboration in assessing impact.
- Decide whether this should be a local or network-wide policy
- Calculate the financial impact for Pharmacy and Clinical directorates.
- Identify additional storage space requirements including refrigerator space as this can be significant
- Remember 'out-sourcing' of banded products has significant additional workload implications which may involve aseptic unit staff (Ordering, goods receipt & reconciliation, Q.A. assessment and release, stock management, documentation of unlicensed products (if batched), incorporation into e-prescribing systems, over-labelling for issue to patients and audit trail of dispensing).
- Draw up a project plan of the phasing/timing of implementation (Unit size and workload will influence whether banding is introduced for all suitable drugs across all tumour sites, or by starting with a few regimens, one tumour site, or a few drugs and build from there).
- Write Proposal or Full Business Case – if required. ([See example - Appendix 4](#))

8.2 Gaining consensus and consent

- Identify a pharmacy project manager to lead the introduction of dose banding.
- Identify a local champion to drive the change process, evangelise and positively motivate everyone.
- Prepare well, research the evidence base, and consider both the positive and negative aspects of the change, in order to be able to answer concerns.
- Engage key stakeholders and obtain their approval. (Mainly those who understand the context and are directly affected by the change, for example: Aseptic Unit Staff, Clinical directors in Oncology & Haematology, Cancer manager, Lead Onc/Haem Nurses, Chief Pharmacist, Network Pharmacist).

8.3 Clinical Governance

- Write a clear policy defining dose bands and the limits and use of banded products.
- Write SOPs for stock control and dispensing processes
- Define your Q.A. procedures in relation to banded products ([See Appendix 5](#))
- Agree an evidence-based shelf-life for each product and include in tender specification
- Draw up contracts with any external suppliers with formal tenders if necessary.
- Involve PASA to negotiate network/regional contract prices as appropriate and include larger NHS manufacturing units in tendering invitations. (See Section 9).
- Record and investigate any errors or untoward incidents to ensure that use of dose banding has not introduced any new systematic errors or risks.

8.4 Training and communication

- Ensure that all relevant prescribers understand the method of prescribing banded doses for appropriate regimens.
- Set up training sessions for rotational or locum staff
- Communicate change thoroughly with all affected prescribers, nurses and pharmacy staff.
- Ensure access to dose banding charts in both paper and electronic format in all relevant clinical areas.
- Establish a schedule for review of dose banding practice.

8.5 Audit

- Audit the outcome of implementation to assess true impact, wastage, whether benefits have been achieved or any unforeseen problems created.
- Publish significant findings

9. Financial and contracting considerations

Savings can be made by negotiation of bulk contracts for pre-prepared chemotherapy on a network, regional or national basis. In small units, any increases in unit dose costs resulting from out-sourced chemotherapy must be set in the context of greater patient convenience and service efficiency.

For implementation to be successful the following must be clear:

- Geographical limits of the banding scheme (Trust, Regional, National)
- Source of banded products (out-sourced or prepared in-house?)
- Local 'drivers' for implementation (Capacity? Patient safety? Financial savings?)
- Contract structure – service only, or procurement of both products and service
- Contract specification details

A sub-group of the National Pharmaceutical Supply Group (NPSG) has been set up to consider the implications of a national contract for dose banded products on the present market and procurement structure for chemotherapy products. The sub-group has the following remit:

- To agree a national standard specification for dose banding
- To understand, document and mitigate the market risks of contracting for dose banding services
- To understand and document the implications on existing contracts for component medicines and to develop a future management strategy
- To develop strategies to ensure that the growth of outsourcing dose banded services does not have a detrimental effect on hospital based manufacturing

It is advisable to seek an update from this group prior to setting up a dose banding contract to ensure you have all available national guidance and documentation. Please contact Beth Loudon at NHS PASA – beth.loudon@pasa.nhs.uk

10. The practicalities of dose bands – deciding band structure, using bands to prescribe, dispense and administer chemotherapy.

10.1 Band structure

Although common principles are used, there is no standardised method of assigning dose bands and there are slight variations in bands adopted by individual cancer networks. As shown in Appendix 3, the determinants of dose bands are the dose/m², the limits of variance from the calculated dose ($\pm 5\%$), the strength of the drug formulation (mg/ml), the agreed maximum number of syringes per dose, maximum fill-volume per syringe or other physical constraints inherent in delivery devices for fixed duration infusions. Banding may also be constrained by limits within electronic prescribing systems.

Commercial suppliers can usually provide any desired dose quantity to accommodate banding.

What degree of precision is necessary given the imprecision of BSA based dosing?

Variance of $\pm 5\%$ is chosen as an acceptable limit to minimise introduction of further error. The examples in Appendix 3 take account of the implied rounding of BSA that occurs when calculating BSA to one decimal place. Maximum variance associated with rounding decisions within a band is also calculated. This provides transparency to prescribers during the approval phase of the banding scheme. Banding schemes based on BSA to one decimal place which do not account for rounding can obscure variances as high as 7 or 8% at the extremes of the rounded range.

What's the best method of choosing the band structure?

There are two general methods of assigning dose bands, both are illustrated in [Appendix 3](#)

10.1.1 BSA based banding

(a) Choose a range of BSA for the band, select a mid band dose as the banded dose then adjust banded dose to a 'measurable' dose within $\pm 5\%$ for whole range.

Example:	Drug:	Cyclophosphamide 600mg/m ²
	Band range chosen:	BSA 1.65 to 1.74 m ²
	Banded dose approx.=	BSA of 1.7 m ²
	Banded dose:	1000mg Maximum variance: - 4.4%

Advantage: Consistent band range.

Disadvantage: Can result in narrow dose bands or unusual banded doses

(b) Choice of a different 'measurable' dose for a BSA band and adjustment of the band range to include +/- 5%

Example: Drug: Cyclophosphamide 600mg/ m²
 Band: around BSA = 1.7 m²
 Banded dose: 1020mg
 Band range: BSA 1.66 to 1.75 m² Maximum variance: -2.9

Advantage: Easily measurable doses. Less variance?

Disadvantage: BSA band range differs between each dose/m² of a specific drug.

10.1.2. 'Target dose' based banding

This method creates a single table for each drug across all common dose/ m² ranges used in various regimens indicating a banded dose within +/- 5% of the calculated dose.

Advantage: No need to create specific dose banding tables for each regimen.
 Easier to maintain bands.
 Consistency across regimens.
 Easier for prescribers?
 Dose modifications are more transparent and straightforward.
 Less risk of a 20% dose reduction being lost or obscured by an upward banding decision.

Disadvantage: May lead to a wide range of banded doses.

10.2 Prescribing

Prescribers should:

- Calculate BSA using one agreed formula and round BSA to one decimal place
- Calculate the dose/ m²
- Chose the nearest banded dose (in the charts provided) in accordance with patient's clinical status.
- Prescribe the banded dose

(In some units banding is incorporated into e-prescribing systems and may be determined by the constraints of the electronic system. In some units using paper-based systems the calculated dose is prescribed and Pharmacists are authorised to select the banded dose and record on the prescription).

10.3 Dispensing

- Prescriptions which have not been banded should be queried with the prescriber.
- Dose banding charts used in Pharmacy can aid product selection by including details of syringe size selection & quantities for each banded dose.
- Design SOPs to ensure clear labelling, assembly and packaging. Grouping together constituent syringes which constitute one dose, and doses which constitute a regimen cycle, for an individual patient.

- Transportation of patients' chemotherapy must be logged and tracked, whether in-house or external.

10.4 Administration

Nurses should:

- Check all banded doses for the patient's chemo cycle are present on receipt
- Store all chemotherapy under correct conditions on receipt, prior to administration
- Leave outer packaging of pre-prepared doses intact until administration is confirmed
- Return unused doses promptly to Pharmacy

11. Frequently Asked Questions

- Q. What if all clinicians do not agree to implement dose banding?
A. Under these circumstances it may be possible to introduce banding on a limited basis for certain specialties or regimens. This is not ideal. If banding is implemented on a restricted basis clear communication of the restrictions is paramount.
- Q. Will I need more storage space?
A. Where banding is adopted additional space for refrigerated and room temperature storage will be needed in order to maximise the benefits of extended shelf-lives of banded doses. Lead times for out-sourcing may increase the amount of pre-prepared doses held in stock.
- Q. How can wastage be minimised?
A. Systems must be in place to ensure correct storage of chemotherapy delivered to chemotherapy day units, cold chain integrity and prompt return of any unused doses. Dedicated Technician time to manage this is essential. Only purchase banded doses as batched products if they have a high frequency of use.
- Q. What is the licensed status of batch-produced chemotherapy doses?
A. Batch-produced doses are unlicensed products. Prescribers and Pharmacists must be aware of their specific responsibilities with regard to unlicensed medicines. Documentation must provide a full audit trail of source materials, manufacture and dispensing to individual patients. Local Q.A. procedures for unlicensed products must be adhered to. (See Appendix 5).
- Q. What is the key to successful implementation?
A. Careful planning, rational choice of dose bands, 'ownership' by all professional groups – not just seen as a Pharmacy initiative, thorough training and ... communication, communication, communication...
Sometimes capacity issues or other resource pressures will drive implementation.

12. Areas for Future Research

Some suggestions:

- Collaborative research into the effect of dose banding on clinical outcomes.
- Population based studies to identify predictive factors for drug pharmacokinetics or therapeutic effect of fixed dose chemotherapy. ⁽³⁾
- Optimal chemotherapy dosing in obesity and cachexia.
- Improving the rationality of chemotherapy dosing schedules
- Better quantitative methods or markers to prospectively predict therapeutic outcome of chemotherapy regimens.
- Collaboration with industry to improve the efficiency of chemotherapy administration.
- More published research into the stability of chemotherapy in syringes and infusion devices.
- Quantitative evaluation of the impact of dose banding on demand and capacity in pharmacy aseptic units and chemotherapy day units. (C-PORT should facilitate this).

13. Bibliography


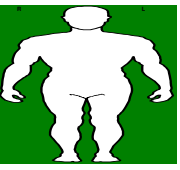
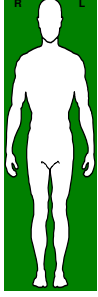
1. Plumridge RJ, Sewell GJ. Dose banding of cytotoxic drugs: a new concept in cancer chemotherapy. *Am J Health-Syst Pharm* 2001; 58:1760 -1764
2. Kaestner SA, Sewell GJ. Chemotherapy dosing Part I; Scientific basis for current practice and the use of body surface area. *Clinical Oncology* 2007; 19:23-37
3. Kaestner SA, Sewell GJ. Chemotherapy dosing Part II; Alternative approaches and future prospects. *Clinical Oncology* 2007; 19: 99-107
4. Du Bois D, Du Bois EF. A formula to estimate the approximate surface area if height and weight be known. *Arch Intern Med* 1916; 17: 863-871
5. Kaestner S, Walker V, Roberts S, Perren T, Sewell G. Clinical and pharmacokinetic (pk) study on 'dose-banded' and individual-dose chemotherapy; an interim report. *J Oncol Pharm Pract* 2004; 10:100.
6. National Dose Banding Survey Results. 2006. Cancer Network Pharmacists Forum
7. Maclean F, Macintyre J, McDade J, Moyes D. Dose banding of chemotherapy in the Edinburgh Cancer Centre. *Pharmaceutical Journal* 17th May 2003; 270: 691-693
8. Summerhayes M. Risk management in oncology. *Pharmaceutical Journal* 11th Nov 2001; 58: 732-733
9. Baker J, Jones S. Rationalisation of chemotherapy services in the University Hospital Birmingham NHS Trust. *J Oncol Pharm Pract* 1998; 4: 10-14
10. Mosteller RD. Simplified calculation of body-surface area. *New Eng J Med* 1987;317:1987 (letter)
11. Haycock GB, Schwartz GJ, Wisotsky DH. Geometric method for measuring body surface area. A height-weight formula validated in infants, children and adults. *J Pediatr* 1978;93(1): 62-66
12. Gehan EA, George SL. Estimation of human body surface area from height and weight. *Cancer Chemother Rep* 1970; 54: 225-235
13. Boyd E, Scammon RE, Lawrence D. The determination of surface area in living children. *Proc Soc Exp Biol Med* 1930; 27:445-449
14. Boyd E. The growth of the surface area of the human body. Minneapolis:University of Minnesota Press. 1935 (www.ispub.com/journals/IJA/Vol2N2/bsa.htm).
15. Personal communications from Nigel Ballantine, Lead Cancer Pharmacist and Dr. Martin English, Consultant Paediatrician, Birmingham Children's Hospital.

Appendix 1. Body Surface Area Calculations and associated variance

Formulae:

DuBois & DuBois ⁽⁴⁾	$\text{BSA (m}^2\text{)} = 0.20247 \times \text{Height(m)}^{0.725} \times \text{Weight(kg)}^{0.425}$ <p>A variation of DuBois and DuBois that gives virtually identical results is: $\text{BSA (m}^2\text{)} = 0.007184 \times \text{Height(cm)}^{0.725} \times \text{Weight(kg)}^{0.425}$</p>
Mosteller ⁽¹⁰⁾	$\text{BSA (m}^2\text{)} = ([\text{Height(cm)} \times \text{Weight(kg)}] / 3600)^{1/2}$ <p>i.e. $\text{BSA (m}^2\text{)} = \text{Square root of } ((\text{cm} \times \text{kg}) / 3600)$</p>
Haycock ⁽¹¹⁾	$\text{BSA (m}^2\text{)} = 0.024265 \times \text{Height(cm)}^{0.3964} \times \text{Weight(kg)}^{0.5378}$
Gehan & George ⁽¹²⁾	$\text{BSA (m}^2\text{)} = 0.0235 \times \text{Height(cm)}^{0.42246} \times \text{Weight(kg)}^{0.51456}$
Boyd ^(13,14)	$\text{BSA (m}^2\text{)} = 0.0003207 \times \text{Height(cm)}^{0.3} \times \text{Weight(grams)}^{(0.7285 - (0.0188 \times \log(\text{grams}))}$

Comparison of BSA Formulae Results

		Variance from the mean of results (%)		Variance from the mean of results (%)		Variance from the mean of results (%)
Ht (m)	1.7		1.4		2.0	
Wt (kg)	75		120		60	
BSA - Dubois	1.86 m ²	-1.59	1.98 m ²	-9.59	1.91 m ²	+4.95
BSA - Mosteller	1.88 m ²	-0.53	2.16 m ²	-1.37	1.82 m ²	0
BSA - Haycock	1.89 m ²	0	2.26 m ²	+3.19	1.79 m ²	-1.65
BSA - Gehan & George	1.90 m ²	+0.53	2.23 m ²	+1.83	1.81 m ²	-0.55
BSA - Boyd	1.91 m ²	+1.06	2.32 m ²	+5.94	1.77 m ²	-2.75
Mean	1.89 m²		2.19 m²		1.82 m²	

Note: Variance between formulae is greatest for short 'stocky' individuals (-9.59% to +5.94%) but in practice BSA may be capped at 2.2 unless the body weight is muscle. Variance may approach 5% in tall thin individuals. This inherent variance is hidden by rounding BSA to one decimal place.

Variance introduced by rounding BSA to one decimal place

BSA Range (m ²)	Rounded to	Variance	Mean Variance	% Variance In BSA
1.31 to 1.35	1.3	-0.01 to -0.05	-0.03	-0.76 to -3.70
1.36 to 1.40	1.4	+0.04 to +0.01	+0.025	+2.94 to +0.71
1.41 to 1.45	1.4	-0.01 to -0.05	-0.03	-0.70 to -3.44
1.46 to 1.50	1.5	+0.04 to +0.01	+0.025	+2.73 to +0.69
1.66 to 1.70	1.7	+0.04 to +0.01	+0.025	+2.40 to +0.58
1.71 to 1.75	1.7	-0.01 to -0.05	-0.03	-0.58 to -2.85
1.81 to 1.85	1.8	-0.01 to -0.05	-0.03	-0.55 to -2.70
1.86 to 1.90	1.9	+0.04 to +0.01	+0.025	+2.15 to +0.52
1.91 to 1.95	1.9	-0.01 to -0.05	-0.03	-0.52 to -2.56
1.96 to 2.00	2.0	+0.04 to +0.01	+0.025	+2.04 to +0.50

Note: Rounding down or up to one decimal place may introduce a variance of approx. 3% in small individuals, approx. 2.5% in average individuals and approx. 2% in large individuals.

Variance of oral dosage forms from the calculated dose/m² as a result of using fixed dosage (capsule strengths) - using Capecitabine as an example

Dosage 1250mg/ m ² twice daily (colorectal and breast cancer)			
BSA (m ²)	Calculated daily dose (mg)	Daily dose in capsules (mg)	Variance (%)
≤1.26	3150	3000	-4.8
1.27 – 1.38	3175 - 3450	3300	+3.9 to -4.3
1.39 – 1.52	3475 – 3800	3600	+3.6 to -5.3
1.53 – 1.66	3825 - 4150	4000	+4.6 to -3.6
1.67 – 1.78	4175 - 4450	4300	+2.9 to -3.4
1.79 – 1.92	4475 - 4800	4600	+2.8 to -4.2
1.93 – 2.06	4825 - 5150	5000	+3.6 to -2.9
2.07 – 2.18	5175 – 5450	5300	+2.4 to -2.7
≥ 2.19	5475	5600	+2.3

Dosage 1000mg/ m ² twice daily (gastric cancer)			
BSA (m ²)	Calculated daily dose (mg)	Daily dose in capsules (mg)	Variance (%)
≤1.26	2520	2300	-8.7
1.27 – 1.38	2540-2760	2600	+2.4 to -5.8
1.39 – 1.52	2780-3040	2900	+4.3 to -4.6
1.53 – 1.66	3060-3320	3200	+4.6 to -3.6
1.67 – 1.78	3340-3560	3500	+4.8 to -1.7
1.79 – 1.92	3580-3840	3600	+0.6 to -6.2
1.93 – 2.06	3860-4120	4000	+3.6 to -2.9
2.07 – 2.18	4140-4360	4300	+3.9 to -1.4
≥ 2.19	4380	4600	+5.0

Appendix 2. Factors affecting clinical outcome of chemotherapy

These are self-evident but serve to illustrate the complexity of any multivariate analyses in this area.

Patient Factors:

Performance status; co-morbidities or concomitant disease states or drug therapy; renal and hepatic function – including activity of metabolising enzymes; gender; age; body size; cancer (genetic) risk status; effects of treatment related toxicities on quality of life.

Tumour factors:

Tumour grade, stage and histology; drug resistance and previous exposure to chemotherapy; vascularity; homogeneity; genotype; immuno-phenotyping - presence or absence of cellular targets or hormonal receptors; cytogenetic markers; gene expression profile.

Chemotherapy Factors:

Treatment intent (neo-adjuvant, adjuvant, palliative or curative); method of administration; regimen & scheduling; dose-intensity delivered (delays in treatment, dose reductions during treatment, use of supportive treatments such as GCSF); respective contribution of individual drugs in a regimen.

Treatment Factors:

Effects of surgery; effect of concurrent or sequential radiotherapy; effect of hormonal or targeted treatments; prognostic expectations at commencement of treatment.

Appendix 3. Examples of Banded drugs and regimens

Any drug which is dosed in mg/m^2 , has documented long term stability and is a high usage item is a candidate for dose banding. Common examples are given below.

Drugs

capecitabine, cyclophosphamide, doxorubicin, epirubicin, fluorouracil, gemcitabine, methotrexate.

Regimens

Regimen specific charts can be developed from dose banding tables for individual drugs. These can be adapted to aid prescribers in dosing decisions or to aid pharmacy and nursing staff in selection of the correct syringe sizes for a banded dose.

Banding tables

Choice of dose bands is defined by locally agreed limits on maximum syringe fill-volume (For example: for vesicant drugs - not more than 40ml in a 60ml syringe) and maximum number of syringes per bolus dose. If fill volume of 50ml in 60ml is used the number of syringes per dose is reduced but this is balanced against risk of repetitive strain injury and hazard of manipulating large syringes of vesicant drugs.

Some illustrative examples are given here. After local discussion, you may wish to adopt a system already in use or design your own dose bands.

Method 1(a) – BSA based banding

The examples given below have been adapted from banding tables used in Scotland.

Cyclophosphamide Dose Bands							
		Dose mg/m^2					
		500		600		750	
BSA (m^2)	BSA Range	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)
1.4	1.40-1.44	700	-2.7	850	-1.6	1100	+4.8
1.5	1.45-1.54	750	+3.4	900	+3.4	1100	-4.8
1.6	1.55-1.64	800	+3.2	950	-3.5	1200	+3.2
1.7	1.65-1.74	850	+3.0	1000	-4.2	1300	+5.1
1.8	1.75-1.84	900	+2.9	1100	+4.8	1350	+2.9
1.9	1.85-1.94	950	+2.7	1150	+3.6	1400	-3.8
2.0	1.95-2.04	1000	+2.6	1200	+2.6	1500	+2.6
2.1	2.05-2.14	1050	+2.4	1250	-2.6	1600	+4.1
2.2	2.15-2.2	1100	+2.3	1300	+0.7	1600	-3.0
Syringe Sizes: 100mg, 300mg, 400mg, 500mg, 600mg, 750mg, 800mg							

Doxorubicin Dose Bands							
Dose mg/m²							
		50		60		75	
BSA (m²)	BSA Range	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)
1.4	1.40-1.44	70	-2.7	85	-1.6	110	+4.8
1.5	1.45-1.54	75	+3.4	90	+3.4	110	-4.8
1.6	1.55-1.64	80	+3.2	95	-3.5	120	+3.2
1.7	1.65-1.74	85	+3.0	100	-4.2	130	+5.1
1.8	1.75-1.84	90	+2.9	110	+4.8	135	+2.9
1.9	1.85-1.94	95	+2.7	115	+3.6	140	-3.8
2.0	1.95-2.04	100	+2.6	120	+2.6	150	+2.6
2.1	2.05-2.14	105	+2.4	125	-2.6	160	+4.1
2.2	2.15-2.2	110	+2.3	130	+0.7	165	+2.3

Syringe Sizes: 10mg, 20mg, 30mg, 40mg, 50mg, 60mg, 75mg, 80mg

Epirubicin Dose Bands									
Dose mg/m²									
		30		50		60		100	
BSA (m²)	BSA Range	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)
1.4	1.40-1.44	42	-2.8	70	-2.8	85	-1.6	140	-2.8
1.5	1.45-1.54	45	+3.4	75	+3.4	90	+3.4	150	+3.4
1.6	1.55-1.64	48	+3.2	80	+3.2	95	-3.5	160	+3.2
1.7	1.65-1.74	50	-4.2	85	+3.0	100	-4.2	170	+3.0
1.8	1.75-1.84	55	-4.8	90	+2.9	110	+4.8	180	+2.9
1.9	1.85-1.94	58	+4.5	95	+2.7	115	+3.6	190	+2.7
2.0	1.95-2.04	60	+2.6	100	+2.6	120	+2.6	200	+2.6
2.1	2.05-2.14	62	-3.4	105	+2.4	125	-2.6	210	+2.4
2.2	2.15-2.2	65	+2.3	110	+2.3	130	-1.5	220	+2.3

Syringe Sizes: 15mg, 20mg, 25mg, 30mg, 40mg, 42mg, 48mg, 50mg, 58mg, 60mg, 62mg, 80mg

Fluorouracil Dose Bands									
Dose mg/m²									
		300		370		425		600	
BSA (m²)	BSA Range	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)
1.4	1.40-1.44	425	-1.6	525	-1.5	600	-2.0	850	-1.6
1.5	1.45-1.54	450	+3.4	550	-3.5	625	-4.5	900	+3.4
1.6	1.55-1.64	475	-3.5	600	+4.6	675	-3.2	950	-3.5
1.7	1.65-1.74	500	-4.2	625	-2.9	725	+3.4	1000	-4.2
1.8	1.75-1.84	550	+4.8	675	+4.2	750	-4.1	1100	+4.8
1.9	1.85-1.94	575	+3.6	700	-2.5	800	-3.0	1125	-3.4
2.0	1.95-2.04	600	+2.6	750	+4.0	850	+2.6	1200	+2.6
2.1	2.05-2.14	650	+3.2	775	+2.1	900	+3.3	1275	+3.7
2.2	2.15-2.2	650	-1.5	800	-1.7	950	+4.0	1300	-1.5

Syringe Sizes: 125mg, 150mg, 300mg, 400mg, 450mg, 475mg, 500mg, 600mg, 650mg, 675mg, 1000mg

Fluorouracil Infusion Dose Bands													
		Dose mg/m ²											
		350		400		500		1400 Over 7 days 200mg/m ² /day		2100 Over 7 days 300mg/m ² /day		2400 Modified De Gramont	
BSA (m ²)	BSA Range	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)
1.4	1.40-1.44	500	+2.0	550	-4.5	700	-2.8	2000	+2.0	3000	+2.0	3500	+4.2
1.5	1.45-1.54	550	+4.8	600	+3.4	750	+3.4	2100	+3.4	3100	-4.1	3600	+3.4
1.6	1.55-1.64	550	-4.2	650	+4.8	800	+3.2	2200	-4.2	3400	+4.5	3800	-3.5
1.7	1.65-1.74	600	+3.9	675	-3.0	850	+3.0	2400	+3.9	3500	-4.2	4000	-4.2
1.8	1.75-1.84	625	-3.0	700	-4.9	900	+2.9	2500	-3.0	3700	-4.2	4300	-2.6
1.9	1.85-1.94	650	-4.3	750	-3.4	950	+2.7	2700	+4.2	3900	-4.3	4500	-3.3
2.0	1.95-2.04	700	+2.6	800	+3.8	1000	+2.6	2800	+2.6	4200	+2.6	4800	+2.6
2.1	2.05-2.14	750	+4.5	850	+3.7	1050	+2.4	3000	+4.7	4400	+2.2	5000	-2.6
2.2	2.15-2.2	750	-2.6	900	+4.7	1100	+2.3	3100	+3.0	4600	+1.9	5300	+2.7

Methotrexate Dose Bands					
		Dose mg/m ²			
		40		50	
BSA (m ²)	BSA Range	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)
1.4	1.40-1.44	55	-4.5	70	-2.8
1.5	1.45-1.54	60	+3.4	75	+3.4
1.6	1.55-1.64	65	+4.8	80	+3.2
1.7	1.65-1.74	67.5	-3.0	85	+2.7
1.8	1.75-1.84	70	-4.9	90	+2.9
1.9	1.85-1.94	75	-3.4	95	+2.7
2.0	1.95-2.04	80	+2.6	100	+2.6
2.1	2.05-2.14	85	+3.7	105	+2.4
2.2	2.15-2.2	90	+4.7	110	+2.3

		Folinic Acid Dose Bands		Gemcitabine Dose Bands			
		Dose mg/m ²		Dose mg/m ²			
		20		1000		1250	
BSA (m ²)	BSA Range	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)	Dose (mg)	Variance % (Max)
1.4	1.40-1.44	30	+7.1	1400	-2.8	1800	+2.9
1.5	1.45-1.54	30	+3.4	1500	+3.4	1900	+4.8
1.6	1.55-1.64	30	+8.5	1600	+3.2	2000	+3.2
1.7	1.65-1.74	35	+6.0	1700	+3.0	2100	-3.4
1.8	1.75-1.84	35	-4.9	1800	+2.9	2300	+5.1
1.9	1.85-1.94	40	+8.0	1900	+2.7	2400	+3.8
2.0	1.95-2.04	40	+2.6	2000	+2.6	2500	+2.6
2.1	2.05-2.14	40	-6.5	2100	+2.4	2600	-2.8
2.2	2.15-2.2	45	+4.7	2200	+2.3	2700	-1.8

Example Breast Cancer Regimen**FEC regimen including syringe sizes**

5-Fluorouracil	600mg/m ² IV bolus day 1
Epirubicin	60mg/m ² IV bolus day 1
Cyclophosphamide	600mg/ m ² IV bolus day 1 (every 21 days for a max. 6 cycles)

BSA (m ²)	5-Fluorouracil 600mg/m ²	Epirubicin 60mg/m ²	Cyclophosphamide 600mg/m ²
1.4	850 (200 +650)	85 (25 +60)	850 (100 + 750)
1.5	900 (400 +500)	90 (30 + 60)	900 (100 + 800)
1.6	950 (300 + 650)	95 (15 + 20 + 60)	950 (100 + 100 + 750)
1.7	1000 (500 + 500)	100 (50 + 50)	1000 (500 + 500)
1.8	1100 (500 +600)	110 (50 +60)	1100 (500 + 600)
1.9	1125 (500 + 500 + 125)	115 (15 + 50 +50)	1150 (400 +750)
2.0	1200 (600 + 600)	120 (60 +60)	1200 (600 + 600)
2.1	1275 (400 + 400 + 275)	125 (25 + 50 + 50)	1250 (500 + 750)
2.2	1300 (650 + 650)	130 (30 + 50 +50)	1300 (500 + 800)

Note: Maximum fill volume 40ml in 60ml syringe. If fill volume of 50ml in 60ml is used number of syringes per dose is reduced but this is balanced against risk of repetitive strain injury and hazard of manipulating large syringes of vesicant drugs.

Method 1(b) BSA based banding

The examples below are from the Black Country Cancer Network:

Black Country Cancer Network**Fluorouracil and Folinic Acid Dose Banding Schedules with % Variance**

- **5FU 300mg/m² + Folinic Acid**

Surface Area (m ²)	5FU Dosage (mg)	Min. Calculated dose (mg)	% below standard dosage	Max. calculated dosage (mg)	% above standard dosage
Up to 1.41	400			423	5.75
1.42 – 1.57	450	426	5.3	471	4.67
1.58 – 1.74	500	474	5.2	522	4.4
1.75 – 1.91	550	525	4.5	573	4.18
1.92 +	600	576	4		

- **5FU 350mg/m² + Folinic Acid**

Surface Area (m ²)	5FU Drug Dosage (mg)	Min. Calculated dose (mg)	% below standard dosage	Max. calculated dosage (mg)	% above standard dosage
Up to 1.35	450			472.5	5
1.36 – 1.5	500	476	4.8	525	5
1.51 – 1.64	550	528.5	3.9	574	4.4
1.65 – 1.78	600	577.5	3.75	623	3.8
1.79 – 1.92	650	626.5	3.6	672	3.4
1.93+	700	675.5	3.5		

- **5FU 370mg/m² + Folinic Acid**

Surface Area (m ²)	5FU Dosage (mg)	Min. Calculated dose (mg)	% below standard dosage	Max. calculated dosage (mg)	% above standard dosage
Up to 1.41	500			521.7	4.3
1.42 – 1.55	550	525.4	4.47	573.5	4.27
1.56 – 1.68	600	577.2	3.8	621.6	3.6
1.69 – 1.82	650	625.3	3.8	673.4	3.6
1.83 – 1.95	700	677.1	3.27	721.5	3.07
1.96+	750	725.2	3.3		

- **5FU 425mg/m² + Folinic Acid**

Surface Area (m ²)	5FU Dosage (mg)	Min. Calculated dose (mg)	% below standard dosage	Max. calculated dosage (mg)	% above standard dosage
Up to 1.35	550			573.8	4.3
1.36 – 1.47	600	578	3.67	624.75	4.1
1.48 – 1.58	650	629	3.23	671.5	3.3
1.59 – 1.7	700	675.8	3.46	722.5	3.2
1.71 – 1.82	750	726.8	3.1	773.5	3.1
1.83 – 1.94	800	777.8	2.78	824.5	3.06
1.95+	850	828.8	2.5		

Black Country Cancer Network**CMF Classical/Modified and FEC Dose-Banding Schedules with % Variances**

- **Cyclophosphamide IV 600mg/m²**

Surface Area (m ²)	Cyclophosphamide Dosage (mg)	Min. Calculated dose (mg)	% below standard dosage	Max. calculated dosage (mg)	% above standard dosage
1.35 – 1.45	840	810	3.57	870	3.57
1.46 – 1.55	900	876	2.66	930	3.33
1.56 – 1.65	960	936	2.50	990	3.13
1.66 – 1.75	1020	996	2.35	1050	2.94
1.76 – 1.85	1080	1056	2.22	1110	2.78
1.86 – 1.95	1140	1116	2.11	1170	2.63
1.96 – 2.0	1200	1176	2.00	1200	-

- **Fluorouracil IV 600mg/m²**

Surface Area (m ²)	5 FU Dosage (mg)	Min. Calculated dose (mg)	% below standard dosage	Max. calculated dosage (mg)	% above standard dosage
1.40 – 1.45	850	840	1.17	870	2.57
1.46 – 1.55	900	876	2.66	930	3.33
1.56 – 1.65	950	936	1.47	990	4.21
1.66 – 1.75	1025	996	2.83	1050	2.43
1.76 – 1.85	1075	1056	1.76	1110	3.25
1.86 – 1.95	1150	1116	2.90	1170	1.73
1.96 – 2.0	1200	1176	2.00	1200	-

Black Country Cancer Network**CMF Classical/Modified and FEC Dose-Banding Schedules with % Variances**• **Methotrexate IV 40mg/m²**

Surface Area (m ²)	Methotrexate Dosage (mg)	Min. Calculated dose (mg)	% below standard dosage	Max. calculated dosage (mg)	% above standard dosage
<1.44	55	-	-	57.2	4.00
1.44 – 1.56	60	57.6	4.00	62.4	4.0
1.57 – 1.68	65	62.8	3.38	67.2	3.38
1.69 – 1.81	70	67.6	3.43	72.4	3.43
1.82 – 1.94	75	72.8	2.93	77.6	3.47
>1.94	80	78	2.5	-	-

• **Epirubicin IV 60mg/m² (FEC)**

Surface Area (m ²)	Epirubicin Dosage (mg)	Min. Calculated dose (mg)	% below standard dosage	Max. calculated dosage (mg)	% above standard dosage
1.4 – 1.45	86	84	2.32	87	1.16
1.46 – 1.55	90	87.6	2.67	93	3.33
1.56 – 1.65	96	93.6	2.50	99	3.10
1.66 – 1.75	102	99.6	2.35	105	2.90
1.76 – 1.85	108	105.6	2.22	111	2.77
1.86 – 1.95	114	111.6	2.10	117	2.63
1.96 – 2.0	120	117.6	2.00	120	-

Method 2 'Target dose' based banding

The following examples are from Dorset Cancer Network.

(Please Note: to limit the number of bands, smaller doses in the tables below have greater variance than +/- 5% until the following doses are reached - 550mg for Cyclophosphamide 45mg for Methotrexate and 50mg for Doxorubicin. The clinical acceptability of such larger variances must be agreed with local clinicians).

5FU Bolus Dose Banding

Dose Range (mg)	Banded dose (mg)
0 - 164	125
165 - 225	200
226 - 287	250
288 - 364	325
365 - 450	400
451 - 525	500
526 - 578	550
579 - 595	600
596 - 650	625
651 - 675	675
676 - 725	700
726 - 789	750
790 - 850	825
851 - 912	875
913 - 952	950
953 - 1052	1000
1053 - 1071	1100
1072 - 1162	1125
1163 - 1225	1200
1226 - 1275	1250
1276 - 1368	1300

Methotrexate Dose banding

Dose Range (mg)	Banded dose (mg)
0 - 7.5	5
7.6 - 11.2	10
11.3 - 13.7	12.5
13.8 - 17.5	15
17.6 - 22.5	20
22.6 - 27.5	25
27.6 - 32.5	30
32.6 - 37.5	35
37.6 - 42.5	40
42.6 - 47.5	45
47.6 - 52.5	50
52.6 - 57.5	55
57.6 - 61.5	60
61.6 - 65	62.5
65.1 - 70	67.5
70.1 - 73.7	72.5
73.8 - 77.5	75
77.6 - 82.5	80
82.6 - 89.4	85

Cyclophosphamide dose banding

BSA Calculations based on CHOP or FEC - Use Dose Range Column for other Doses

CHOP (750mg/m ²) BSA (m ²)	FEC (600mg/m ²) BSA (m ²)	Dose range (mg)	Banded Dose (mg)
-----	-----	715 - 775	750
-----	-----	776 - 842	800
-----	1.45 - 1.55	858 - 947	900
-----	1.60 - 1.75	953 - 1052	1000
1.45 - 1.55	1.80 - 1.95	1067 - 1178	1120
1.60 - 1.75	2.0 - 2.2	1200 - 1326	1260
1.80 - 1.95	-----	1335 - 1473	1400

DOXORUBICIN dose banding**BSA Calculations for CHOP- Use Dose Range Column for other Doses**

CHOP (50mg/m ²) Surface area (m ²)	Dose range (mg)	Banded dose (mg)
-----	27.6 - 32.5	30
-----	32.6- 37.5	35
-----	37.6 - 42.5	40
-----	42.6- 47.5	45
-----	47.6 - 52.5	50
-----	52.6- 57.5	55
-----	57.6 - 62.5	60
-----	62.6- 67.5	65
1.35 – 1.45	67.6 - 72.5	70
1.46 - 1.54	72.6- 77.5	75
1.55 – 1.64	77.6 – 82.5	80
1.65 – 1.74	82.6 - 87.5	85
1.75 – 1.84	87.6 – 92.5	90
1.85 – 1.94	92.6 – 97.5	95
1.95 – 2.05	97.6 – 102.5	100
2.06 – 2.15	102.6 - 107.5	105
2.16 – 2.3	107.6 – 115	110

The banded dose is within +/- 5% of the original dose for all of the normal doses. Dose reductions below 70mg may have wider band, but not clinically significant. (Syringe sizes available (mg): 30,35,40,45,50,55)

Oral chemotherapy

Capecitabine Dose Banding – Adapted from Peninsula Cancer Network Document					
Capecitabine 1250mg/m² twice daily					
BSA (m²)	Actual dose taken BD	Banded Dose taken BD	Variance%	Tablets taken BD	Total Number of tablets per day
1.5	1875	1800	- 4.0	3 x 500mg 2 x 150mg	10
1.6	2000	2000	0.0	4 x 500mg	8
1.7	2125	2000	- 5.9	4 x 500mg	8
1.8	2250	2300	+2.2	4 x 500mg 2 x 150mg	12
1.9	2375	2500	+5.3	5 x 500mg	10
2.0	2500	2500	0.0	5 x 500mg	10

If you wish to adopt, or adapt, a banding scheme that is already in use rather than formulating your own, the following individuals have very kindly agreed to be contacted:

Name	Job Title	Email address
Steve Williamson	Consultant Pharmacist in Cancer Services North East Cancer Network	Steve.Williamson@nhct.nhs.uk
Mary Maclean	Regional Cancer Care Pharmacist (West of Scotland)	Mary.Maclean@ggc.scot.nhs.uk
Colin Ward	Derby/Burton Cancer Network Lead Pharmacist	Colin.Ward@derbyhospitals.nhs.uk
Martin Rees-Milton	Principal Pharmacist Aseptic Services Velindre Cancer Centre Cardiff (Extensive experience with 'Chemocare') eRx system	Martin.Rees-Milton@velindre-tr.wales.nhs

Appendix 4. Sample Business Case

Brief outlines, at two levels of detail, are suggested below.

1. Change Proposal Outline (Simple)

Subject:	Introduction of Dose banding of Chemotherapy
Purpose:	To rationalise chemotherapy provision, regulate demand and capacity for aseptic services and facilitate national contracting arrangement
Scope:	Trust –wide or Network-wide
Authors/Signatories:	Clinical director of oncology; Clinical director of haematology ; Lead Oncology Pharmacist; Lead Oncology Nurse.
Sponsor:	Director of operations/Director of cancer services
Background –	what has stimulated the proposal, reasons for change
Service now –	individualised dosing, workload, capacity and ‘case-mix’
Method of Dose banding –	explanation in lay terms with simple regimen example and illustrative tables.
Option appraisal -	pro’s and con’s of each option including implementation details, financial and service implications. Use actual local data to create audience interest and impact. Include capital and revenue consequences or savings. Cost comparison of in-house vs out-sourced, if relevant. Include true costs such as transportation fees, emergency order fees, on-costs. Predict annual usage figures based on recent data. Risks and benefits.
Preferred option -	sell the idea!

Business Case Outline (Complex)

Contents

1.Executive summary

2. Strategic case

Introduction

National Context

Local Context

Objectives & Scope

Strategic Benefits

Strategic Risks

Constraints and dependencies

Conclusion

3. Financial/Commercial case/ Economic case

Introduction

Scope

Implementation options

Preferred implementation approach

Costs

Funding

4. Management Case

Introduction

Project Management methodology and structure

Managing risk

Training requirements

Service management

Communications

Post-project evaluation

Appendix 5

Guidance for the purchase and supply of unlicensed medicinal products – notes for prescribers and pharmacists. NPQAC 3rd Edition June 2004

See separate Acrobat (.pdf) document.