MEMORANDUM FOR BOARD MEETING OF 29 JUNE 2005

To: PHARMAC Directors

From: Sean Dougherty

Date: 21 June 2005

OXYCODONE HYDROCHLORIDE

Recommendations

It is recommended that having regard to the decision criteria set out in Section 2.2 of PHARMAC's Operating Policies and Procedures you:

resolve to list oxycodone hydrochloride in the Opioid Analgesics therapeutic subgroup of Section B and in Part II of Section H of the Pharmaceutical Schedule from 1 August 2005 as follows:

Presentation	Brand	Strength	Pack Size	Price/Subsidy
Capsules	OxyNorm	5 mg	20	$2.83
Capsules	OxyNorm	10 mg	20	$5.58
Capsules	OxyNorm	20 mg	20	$9.77
Controlled-release tablets	OxyContin	10 mg	20	$11.14
Controlled-release tablets	OxyContin	20 mg	20	$18.93
Controlled-release tablets	OxyContin	40 mg	20	$33.29
Controlled-release tablets	OxyContin	80 mg	20	$58.03

resolve to apply the following restriction to the prescribing of oxycodone capsules and controlled-released tablets in Section B of the Pharmaceutical Schedule:

Only on a controlled drug form.

resolve to apply the following guideline to the prescribing of oxycodone capsules and controlled-released tablets in Section B of the Pharmaceutical Schedule:

Prescribing Guideline
Prescribers should note that oxycodone is significantly more expensive than long-acting morphine sulphate and clinical advice suggests that it is reasonable to consider this as a second-line agent to be used after morphine.

note that the agreement provides for the listing of the following presentation should regulatory approval and other consents be granted:

Presentation	Brand	Strength	Pack Size	Price/Subsidy
Controlled-release tablets	OxyContin	5 mg	20	$7.51

resolve to approve the 17 May 2005 agreement with Mundipharma New Zealand Limited in its entirety.

SUMMARY OF PHARMACEUTICAL			
Brand Name	OxyNorm, OxyContin	**Chemical Name**	Oxycodone hydrochloride
		Presentation	Capsules and controlled-release tablets
Therapeutic Group	Opioid analgesics (Nervous System)	**Pharmaceutical Type**	New chemical entity
Supplier	Mundipharma New Zealand Limited	**Application Date**	April 2004
MOH Restrictions	Controlled Drug (B3)		
Current subsidy	Nil		
Proposed subsidy	**Capsules**	**Manufacturer's surcharge**	Nil
	$2.83 per 20		
	$5.58 per 20		
	$9.77 per 20		
	Controlled-release tablets		
	$7.51 per 20		
	$11.14 per 20		
	$18.93 per 20		
	$33.29 per 20		
	$58.03 per 20		
Proposed restriction	Only on a controlled drug form		
OP	No	**Section F**	No

Market data	YE 30 June 2006	YE 30 June 2007	YE 30 June 2008
Subsidy (gross)	$880,000	$1,300,000	$1,800,000
Net cost to Schedule	$620,000	$930,000	$1,200,000
Net cost to DHBs	$620,000	$930,000	$1,200,000
Net cost to DHBs (NPV)	$5,000,000		

Notes:
1. Subsidy (gross) = forecast of spending on oxycodone at the proposed subsidy.
2. Net cost to Schedule = forecast of change in total spending on pharmaceuticals listed on the Schedule compared with status quo.
3. Net cost to DHBs = Net cost to the Schedule.
4. All costs are expressed ex manufacturer, excluding GST.
5. NPV is calculated over 5 years using an annual discount rate of 10%.
6. Calculations in Doc #87725

Executive Summary

Key Issues in the Proposal

- Listing oxycodone, a strong opioid analgesic, in the Pharmaceutical Schedule would provide an alternative treatment option to morphine sulphate tablets and capsules. It has similar efficacy and tolerability, but will allow for opioid rotation and further treatment options when morphine is not tolerated.

- In 2002, the review of analgesic agents by the newly formed Analgesic and Antiemetic Subcommittee of PTAC (now the Analgesic Subcommittee of PTAC) highlighted several gaps in the publicly funded list of analgesic agents; the Subcommittee recommended that PHARMAC list another strong opioid analgesic as an alternative to morphine.

- The Analgesic Review Board paper in April 2005 highlighted further the gaps in analgesia treatment available in New Zealand, and noted that PHARMAC staff were pursuing the listing of oxycodone as an alternative strong opioid analgesic.

- The listing of oxycodone in Section B of the Pharmaceutical Schedule would be associated with a small cost increase in the first few years, with the estimated increase in expenditure in the fifth year being less than $2,000,000.

Why Proposal not decided under Delegated Authority

The proposal outlined in this Board paper has not been dealt with by the CEO under delegated authority because the Board has requested to be involved in all current investment decisions.

The proposal

- Listing oxycodone hydrochloride capsules and controlled-release tablets in Section B and in Part II of Section H of the Pharmaceutical Schedule

- Listing a further presentation of the controlled release tablets at a later time following registration.

Note: an agreement, conditional on consultation and Board approval, between Mundipharma New Zealand Limited and PHARMAC dated 17 May 2005 is attached as Appendix 1.

Estimate of the effects of the proposal

Given the experience of oxycodone in Australia, PHARMAC staff anticipate that the market for oxycodone will grow gradually, increasing market share over long-acting morphine by around 5% per year. Overall market share is anticipated to be:

2006	2007	2008	2009	2010
10%	15%	20%	25%	30%

Short-acting oxycodone

The listing of the short-acting formulation is anticipated to have a minimal effect on the pharmaceutical budget. Its pricing is substantially lower per tablet than the equivalent dose of short-acting formulations of morphine sulphate, viz:

Oxycodone		Morphine	
5 mg	$0.14	10 mg	$0.26
10 mg	$0.28	20 mg	$0.51
20 mg	$0.49	40 mg (2 x 20 mg)	$1.02

The effect of listing these presentations is anticipated to have a 50% reduction in expenditure over the share of the market that shifts to oxycodone.

	2006	2007	2008	2009	2010
Morphine sulphate – SQ	$520,000	$570,000	$620,000	$660,000	$710,000
Oxycodone market share	10%	15%	20%	25%	30%
Oxycodone	$26,000	$43,000	$62,000	$83,000	$110,000
Savings	$26,000	$43,000	$62,000	$83,000	$110,000

Long-acting oxycodone

Long-acting oxycodone is priced higher than the equivalent morphine sulphate; we anticipate that oxycodone will have an average daily cost of around $4.00, compared with $1.00 for morphine.

	2006	2007	2008	2009	2010
Morphine sulphate – SQ	$2,100,000	$2,100,000	$2,200,000	$2,200,000	$2,200,000
Oxycodone market share	10%	15%	20%	25%	30%
Oxycodone	$860,000	$1,300,000	$1,700,000	$2,200,000	$2,700,000
Costs	$640,000	$970,000	$1,300,000	$1,700,000	$2,000,000

Although costs here have been calculated on an equal dose basis, opioid rotation may mean that incremental costs may be less than considered here. For example, patients may be switched to an equipotent dose of oxycodone rather than having further dose escalation on morphine. While this is unlikely to make oxycodone less expensive than morphine, it would reduce its incremental cost.

Although oxycodone is more expensive than morphine, it is less expensive than fentanyl patches. Many of the patients for whom fentanyl patches are available will be able to take oxycodone, which would in turn result in a cost saving. For example, although the average daily cost of oxycodone is anticipated to be around $4.00, the daily cost of fentanyl patches is currently around $7.50. As both oxycodone and fentanyl are aimed at many of the same patients (opioid-responsive patients intolerant of morphine), the actual incremental costs of long-acting oxycodone could be less than presented here.

PHARMAC Staff View

PHARMAC staff consider that this proposal should be accepted. This proposal will allow for an easily-accessible alternative strong opioid analgesic at little overall cost to the pharmaceutical budget.

This proposal also represents a further step forward in PHARMAC's analgesic strategy that was presented to the Board in April 2005. Following acceptance of this proposal, a majority of the new investments in analgesics will have been completed, with the remaining work primarily involving clinical and pharmacoeconomic assessment, minor derestrictions and subsidy increases for a number of items.

PHARMAC staff consider that there is little long-term financial risk with oxycodone as generic preparations are already available. A generic 5 mg short-acting oxycodone is available in Australia supplied by Sigma Pharmaceuticals, although [redacted]

[redacted]Active sourcing of generic oxycodone by PHARMAC staff may result in generic formulations being available within a few years.

The listing of oxycodone in Part II of Section H provides DHB hospitals with a national contract, but is not expected to significantly alter expenditure in this area.

Background

Oxycodone and its uses

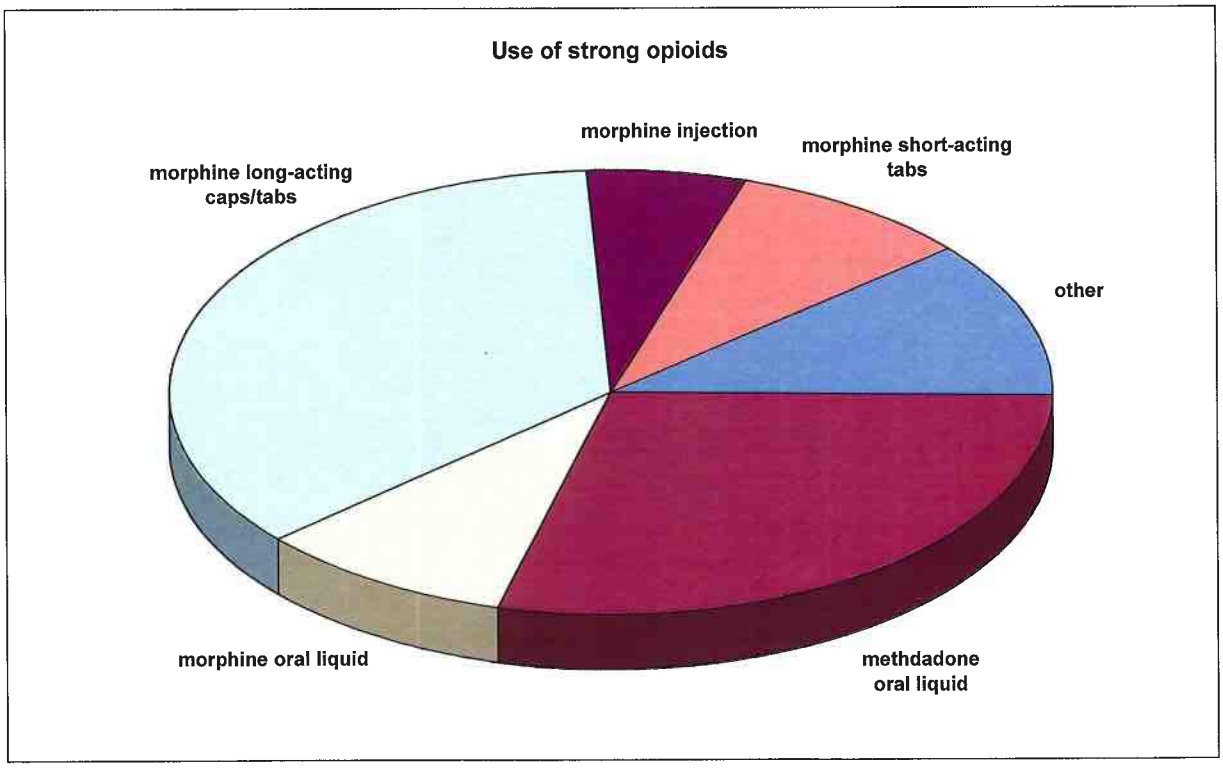
Oxycodone is a strong opioid analgesic agent similar to morphine, and is indicated for the treatment of opioid responsive moderate to severe pain. It has an affinity for kappa, mu, and delta opiate receptors in the brain and spinal cord. The therapeutic effect is mainly analgesic, anxiolytic, antitussive and sedative.

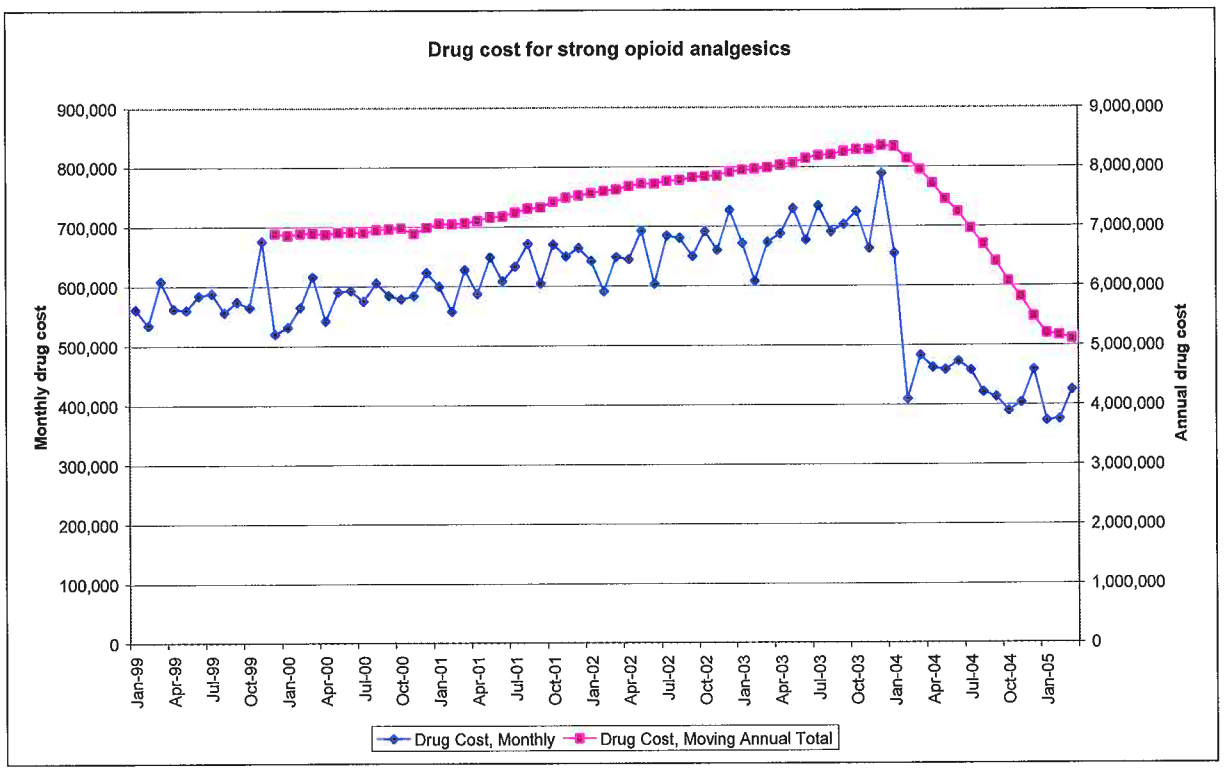
The dynamics of the market for strong opioid analgesics

There are several opioid analgesics listed in the Pharmaceutical Schedule, which can be classified as 'strong' and 'weak' opioids:

Strong Opioids	Morphine
	Methadone
	Buprenorphine
	Fentanyl
	Pethidine
Weak Opioids	Codeine
	Dextropropoxyphene
	Dihydrocodeine

Of the strong opioids, buprenorphine and pethidine are infrequently used in New Zealand, and fentanyl patches have only recently been introduced, and are relatively tightly restricted. The most commonly used formulation for chronic pain is morphine long-acting capsules and tablets (methadone oral liquid is primarily used in treatment of opiate addiction).





The sharp reduction in the cost of strong opioid analgesics in early 2004 is due to reference pricing in the market for long-acting morphine sulphate.

International prices for oxycodone

A comparison of international prices for oxycodone is outlined below:

	Source	Strength	Pack Size	Local Price	Exchange rate	Price ($NZ)
Proposal						
Capsules		5 mg	20			2.83
		10 mg	20			5.58
		20 mg	20			9.77
Controlled-release		5 mg	20			7.51
tablets		10 mg	20			11.14
		20 mg	20			18.93
		40 mg	20			33.29
		80 mg	20			58.03
Australia	PBS					
Capsules		5 mg	20	$2.58	0.9117	2.83
		10 mg	20	$5.09		5.58
		20 mg	20	$8.91		9.77
Controlled-release		5 mg	20	$6.85		7.51
tablets		10 mg	20	$10.15		11.14
		20 mg	20	$17.26		18.93
		40 mg	20	$30.35		33.29
		80 mg	20	$52.90		58.03
United Kingdom	BNF 49					
Capsules		5 mg	56	£9.86	0.3653	26.99

	10 mg	56	£19.72	53.97
	20 mg	56	£39.42	107.92
Controlled-release tablets	5 mg	28	£10.81	29.59
	10 mg	56	£21.60	59.13
	20 mg	56	£43.20	118.26
	40 mg	56	£86.42	236.57
	80 mg	56	£172.84	473.13

Note: Prices are expressed ex manufacturer, excluding GST.

PTAC View

Analgesic Subcommittee of PTAC, 9 September 2002

"The subcommittee considered that there was a clinical need not being met by the products currently listed in this therapeutic group on the Pharmaceutical Schedule. The subcommittee recommended PHARMAC staff explore the possibility of listing tramadol, hydromorphone, oxycodone, fentanyl patches, fentanyl transmucosal and dispersible morphine slow release preparation. The dispersible morphine dissolves completely and part doses can be measured easily. The subcommittee also noted that it also works well in tube feeds.

The subcommittee considered that at least one alternative opioid for strong pain other than morphine is needed that is easy and flexible to titrate, has oral and sc/iv/pr administration routes and is safer to use in renal failure. Hydromorphone would suit this profile as second line for morphine intolerant patients or patients in renal failure.

The subcommittee considered that oxycodone had an efficacy and side-effect profile similar to that of morphine. The subcommittee noted that it was primarily used for control of pain in palliative care. The subcommittee noted that oxycodone was currently available on the Pharmaceutical Schedule in suppositories only (oxycodone pectinate). It is believed that oral oxycodone preparations have a high abuse potential in the United States."

PTAC, 20 May 2004

"The Committee noted that the Analgesic Sub-committee of PTAC had considered that there was a clinical need not being met by the products currently listed in the Analgesic therapeutic group of the Pharmaceutical Schedule and had recommended that PHARMAC staff explore the possibility of listing oxycodone. Members noted that the submission from Mundipharma was in response to PHARMAC staff requesting it.

The Committee considered that the evidence supplied by Mundipharma was adequate, but contained no clinical data comparing oxycodone with other strong opioids. However, it did note that oxycodone appeared to have similar analgesic efficacy to morphine sulphate, and was on the WHO Pain Ladder at Step 3. The Committee asked that more comparative data against other step 3 opioids be supplied by Mundipharma and that other formulations of oxycodone also be included in the application (short acting, liquids and injection).

The Committee considered that oxycodone would replace morphine in times of opioid switching and/or rotation. It considered that morphine sulphate would continue to be used as first-line treatment for palliative care. However, there may approximately 18% of patients currently being treated with morphine who, due to lack of analgesic effect or intolerable adverse effects, may benefit if oxycodone were available.

They noted that oxycodone was more expensive than morphine sulphate in both the UK and in Australia, and that the supplier had not submitted pricing in its application.

The Committee recommended that long-acting oxycodone should be listed on the Pharmaceutical Schedule, and gave this a medium priority. The relevant decision criteria for this recommendation were *(i) The health needs of all eligible people within New Zealand;* as there are some patients currently being treated with morphine who due to lack of analgesic effect or intolerable adverse effects, may benefit if oxycodone were available; and *(iii) The availability and suitability of existing medicines, therapeutic medical devices and related products and related things;* there are some patients for whom there are no suitable alternatives."

Comments from Interested Parties

Section 49(a) requires PHARMAC to consult, when it considers appropriate to do so, on matters that relate to the management of pharmaceutical expenditure with any sections of the public, groups or individuals that, in the view of PHARMAC, may be affected by decisions on those matters.

Accordingly, a consultation letter was circulated on 27 May 2005 to all suppliers and other parties that, in the view of PHARMAC, may be affected by the recommendations contained in this paper.

- Pharmaceutical suppliers
- Interested parties
- Analgesic consultation list

The consultation letter, the distribution list, and all responses received by 17 June 2005 are attached as Appendix 2.

Other affected parties

Murray Tilyard, BPAC and South Link Health

Prof. Tilyard indicated support for the proposal from BPAC and from South Link Health.

Teresa Omundsen, HealthPAC

HealthPAC note that the proposal will be unlikely to have any technical or resource impacts.

Johnathan Adler, Ross Drake, Carol McAllum and Jane Vella-Brincatt, New Zealand Palliative Care Pharmaceutical Group

Dr Adler et al indicated support for the proposal, and indicated support for other presentations of oxycodone to be listed in the future.

PHARMAC staff response

PHARMAC staff note that Mundipharma has submitted dossiers for oxycodone oral liquid and injection to Medsafe, and that PHARMAC will be likely to receive applications from Mundipharma once registration is complete.

Legal advisors' view

Legal advisors' view not sought for this proposal.

Implementation

Section 49(b) requires PHARMAC to take measures to inform the public, groups and individuals of PHARMAC's decisions concerning the pharmaceutical schedule. Accordingly, if the Board adopts the recommendations contained in this paper PHARMAC staff will take the following measures to inform the public, groups and individuals of that decision:

- Notify Mundipharma New Zealand Limited
- Looking Forward – inform Schedule Team
- Communication

  Pharmacy – Dispatch
  Public-media release

DECISION CRITERIA

Set out below is PHARMAC staff's assessment of the application of the decision criteria in section 2.2 of the Operating Policies and Procedures. This assessment is intended for discussion purposes, is not necessarily exhaustive and is not a substitute for the analysis contained in the paper. The Board is not bound to accept PHARMAC staff's assessment of the application under the decision criteria and may attribute different weightings to each of the criteria from those attributed by PHARMAC staff.

(i) *The health needs of all eligible people within New Zealand;*

The analgesic review conducted by PHARMAC highlighted that there are currently treatment gaps in the list of publicly funded analgesic agents, including the strong opioid analgesics. This proposal would provide for a long and short-acting alternative to morphine available without Special Authority.

(ii) *The particular health needs of Maori and Pacific peoples;*

PHARMAC staff consider that Maori and Pacific peoples will benefit from this proposal in equal proportion to the population as a whole.

(iii) *The availability and suitability of existing medicines, therapeutic medical devices and related products and related things;*

Although other strong analgesics are available, only morphine is available as a long-acting oral formulation. Where patients are unable to take morphine, oxycodone represents an alternative to fentanyl patches; oxycodone will also allow for opioid rotation for chronic treatment.

(iv) *The clinical benefits and risks of pharmaceuticals;*

Oxycodone is unlikely to provide an improvement in analgesia over morphine, although for morphine-intolerant patients, or in opioid rotation, it is likely to result in a reduction in side effects.

(v) *The cost-effectiveness of meeting health needs by funding pharmaceuticals rather than using other publicly funded health and disability support services;*

Although no formal cost-utility analysis has been undertaken for this proposal, we note that it is likely that this proposal would be favourable. It is unlikely that oxycodone will be routinely preferred to morphine as a first-line strong opioid analgesic. For those patients where morphine is not tolerated, oxycodone is cheaper than fentanyl patches, the current alternative. If used in opioid rotation, the availability of oxycodone will result in a reduction in opioid-related side effects for patients on long-term opioid treatment.

(vi) *The budgetary impact (in terms of the pharmaceutical budget and the Government's overall health budget) of any changes to the Pharmaceutical Schedule;*

The proposal is anticipated to have a first-year impact on pharmaceutical expenditure of $600,000, increasing to $1,900,000 in the fifth year of listing, a discounted cost of nearly $5,000,000 over the first five years. No impact on non-pharmaceutical health sector expenditure is anticipated.

(vii) *The direct cost to health service users;*

No patient co-payment will apply to the dispensing of oxycodone, so patients will be financially unaffected by this proposal.

(viii) *The Government's priorities for health funding, as set out in any objectives notified by the Crown to PHARMAC, or in PHARMAC's Funding Agreement, or elsewhere; and*

This criterion is not relevant to this proposal.

(ix) *Such other criteria as PHARMAC thinks fit.*

No other criteria are relevant to assessing this proposal.

Checklist for Board papers

Paper: Oxycodone hydrochloride

Date of Board Meeting: 29 June 2005

Consultation:

The following parties were consulted with during the development of this paper

Party	Consulted	Comments
Minister of Health	☐	☐
Ministry of Health	☐	☐
DHBs	☐	☐
PTAC	☐	☐
Consumer Advisory Committee	☐	☐
Affected health professionals (refer to attached distribution list)	☑	☑
Affected patient/consumer groups (refer to attached distribution list)	☑	☐
Affected suppliers (refer to attached distribution list)	☑	☐
Other affected public, groups and/or individuals (specify)	☑	☐

The Author(s) confirm that appropriate processes were followed for the development of this paper, including appropriate consultation and consideration of consultation responses.

Principal Author (sig): _____

Other Authors (sig): _____

Medical director (sig): _____

Peer reviewer (sig): _____
(Takes equal responsibility with the author(s) for all aspects of the paper)

Schedule analyst (sig): _____
(Resolutions checked)

IT manager (sig): _____
(Restrictions checked and XML Form generated and attached where applicable)

Approved for inclusion in Board Agenda:

_____ _____ 23/6/05

Chief Executive **Date**