Guidelines for the diagnosis and treatment of malignant pleural mesothelioma

Administrative Report

January 2013

CONTENTS

Contents of this report relate to the requirements for meeting the NHMRC standard on pages 16-23 of the *Procedures and requirements for meeting the 2011 NHMRC standard for clinical practice guidelines(1)*

A. Governance and stakeholder involvement

A.1 The organisation/s responsible for developing and publishing the guideline is/are named.

Asbestos Diseases Research Institute (ADRI)

A.2 Sources of funding for guideline development, publication and dissemination are stated.

The development of these Guidelines was made possible by: a generous donation from the Biaggio Signorelli Foundation; a Cancer Institute NSW grant; a contribution from Cancer Council NSW and in-kind contributors from the Director, Executive Officer and Admin Support from the Asbestos Diseases Research Institute and the national team of experts involved.

Publication of the Guidelines has been made possible by a grant from Comcare's Asbestos Innovation Fund.

A.3 A multidisciplinary group that includes end-users, relevant disciplines and clinical experts is convened to develop the purposes, scope and content of the guideline, and the process and criteria for selecting member are described.

The initial phase a core group of the Organizing Committee developed the guidelines scope and terms of reference. The Organising Committee convened the first Steering Committee meeting (15th Feb 2010) where the purposes, scope, recommendations regarding the different disciplines that should be represented in the Guidelines Working Groups. From this meeting five working groups were formed with two to three co-chairs per groups nominated. For each working group a list 5-6 relevant disciplines and clinical experts were formulated and subsequently sent a written invitation to join the Group. For each Working Group a consumer representative was also invited to join.

A.4 Consumers participate in the guideline development, and the processes employed to recruit, involve and support consumer participants are described.

The development of the guidelines has been set out in five working groups: Diagnosis, Assessment, Active Therapy, Supportive and Palliative Care and Models of Care. Within each of these working groups a consumer representative has been invited to participate and appointed. The consumer representatives have also been invited and have attended the Steering Committee meetings. Before the draft guidelines are submitted for public consultation they will be reviewed by the groups including the consumer representatives. Public consultation will include a review by consumer organizations such as ADFA (Asbestos Diseases Foundation of Australia).

A.5 A complete list of all the people involved in the guideline development process is provided, including the following information for each person: name, profession or discipline, organisational affiliation and role in the guideline development process.

Table 1. Steering committee

Organising committee		
Dr Andrew Penman (Chair)	Medical administrator	The former CEO, Cancer Council NSW
Ms Victoria Keena	Executive officer	Executive Officer, Asbestos Diseases Research Institute, NSW
Professor Nico van Zandwijk	Thoracic oncologist	Director, Asbestos Diseases Research Institute, NSW Professor, The University of Sydney, NSW
Dr Christopher Clarke	Thoracic physician	Clinical Advisor, Asbestos Diseases Research Institute, NSW
Dr Henry Marshall	Respiratory physician	The Prince Charles Hospital, Department of Thoracic Medicine, Chermside QLD
Dr Steven Leong	Respiratory physician	The Prince Charles Hospital, Department of Thoracic Medicine, Chermside QLD

Co-chairs, Working groups		
Professor Douglas Henderson	Anatomical pathologist	Professor of Anatomical Pathology & Senior Consultant in Surgical Pathology, SA Pathology, Flinders Medical Centre, Bedford Park, SA
Professor AW (Bill) Musk	Respiratory physician	Clinical Professor, Department of Respiratory Medicine, Sir Charles Gairdner Hospital, Nedlands WA Clinical Professor, The University of Western Australia, WA
Professor Kwun Fong	Thoracic & sleep physician	Professor, Thoracic and Sleep Physician, Professor School of Medicine, The University of Queensland, Director UQ Thoracic Research Centre at The Prince Charles Hospital, Chermside QLD
Professor Anna Nowak	Medical oncologist	Professor (Medical Oncology), School of Medicine and Pharmacology, University of Western Australia, Crawley, WA. Medical Oncologist, Sir Charles Gairdner

Co-chairs, Working groups		
		Hospital, Nedlands WA
Dr Robert Loneragan	Radiologist	Staff Specialist, Radiology Department, Concord Hospital, Concord NSW
A/Professor Brian McCaughan	Cardiothoracic surgeon	VMO, Royal Prince Alfred Hospital, Camperdown NSW Clinical Associate Professor of Surgery, The University of Sydney, NSW
Professor Michael Boyer	Medical oncologist	Clinical Professor, Central Clinical School, The University of Sydney, NSW
Dr Malcolm Feigen	Radiation oncologist	Senior Consultant, Austin Hospital, Heidelberg VIC
Professor David Currow	Palliative care specialist	Chief Cancer Officer & CEO, Cancer Institute NSW, Eveleigh NSW
A/Professor Penelope Schofield	Supportive care specialist	NHMRC Research Fellow, Research Director, Department of Nursing and Supportive Care Research, Peter MacCallum Cancer Centre, VIC
Ms Beth Ivimey	Lung cancer nurse coordinator	Prince of Wales Hospital, Randwick, NSW
A/Professor Nick Pavlakis	Medical oncologist	Director of Medical Oncology, Royal North Shore Hospital, NSW Current Chairman of the Scientific Advisory Committee of the Australian Lung Cancer Trials Group.
Ms Jocelyn Mclean	Case manager for thoracic surgery	Cardiothoracic Surgery, Royal Prince Alfred Hospital, Camperdown NSW

Librarians		
Ms Suzanne Bakker	Librarian	Netherlands Cancer Institute (NKI) Amsterdam, The Netherlands
Mr Jeremy Cullis	Librarian	Assistant Manager/Faculty Liaison Librarian (Medical Science Libraries), The University of Sydney NSW
Ms Yaping Liu	Librarian	Cancer Council NSW

Consumer representatives		
Mr Paul Signorelli	Consumer	Director, Doltone House; Director, Biaggio Signorelli Foundation, NSW
Mrs Carol Klintfält	Consumer	Consumer Representative

Mrs Jenny Weismantel	Consumer	Consumer Representative

Table 2. Working groups

Diagnosis		
Professor Douglas Henderson (Co-chair)	Anatomical pathologist	Professor of Anatomical Pathology & Senior Consultant in Surgical Pathology, SA Pathology, Flinders Medical Centre, Bedford Park, SA
Professor AW (Bill) Musk (Co-chair)	Respiratory physician	Clinical Professor, Department of Respiratory Medicine, Sir Charles Gairdner Hospital, Nedlands WA Clinical Professor, The University of Western Australia, WA
Mr Morgan Windsor	Cardiothoracic surgeon	Department of Thoracic Surgery, The Prince Charles Hospital Dept of Thoracic Medicine, Chermside QLD
Dr Richard Slaughter	Radiologist	Chair of Medical Imaging, The Prince Charles Hospital, Chermside QLD
Dr Annabelle Mahar	Anatomical pathologist	Tissue Pathology & Diagnostic Oncology, Royal Prince Alfred Hospital, Camperdown, NSW
Dr Belinda Clarke	Anatomical pathologist	The Prince Charles Hospital, Chermside QLD
Dr Amanda Segal	Anatomical pathologist	Department of Tissue Pathology, PathWest QEII Medical Centre, WA
Dr Roslyn J. Francis	Nuclear medicine specialist	Nuclear Medicine, Sir Charles Gairdner Hospital, Nedlands WA
Ms Beth Ivimey	Lung cancer nurse coordinator	Prince of Wales Hospital, Randwick, NSW
Mr Paul Signorelli	Consumer	Consumer Representative, Director, Doltone House, NSW
Ms Suzanne Bakker	Librarian	Netherlands Cancer Institute (NKI) Amsterdam, The Netherlands

Assessment		
Professor Kwun Fong (Co-chair)	Thoracic & sleep physician	Professor, Thoracic and Sleep Physician, Professor School of Medicine, The University of Queensland, Director UQ Thoracic Research Centre at The Prince Charles Hospital,

		Chermside QLD
Professor Anna Nowak (Co-chair)	Medical oncologist	Professor (Medical Oncology), School of Medicine and Pharmacology, University of Western Australia, Crawley, WA. Medical Oncologist, Sir Charles Gairdner Hospital, Nedlands WA
Dr Robert Loneragan (Co-chair)	Radiologist	Staff Specialist, Radiology Department, Concord Hospital, Concord NSW
A/Professor John Alvarez	Cardiothoracic surgeon	Clinical Associate Professor, University of Western Australia Department of Cardiothoracic Surgery, Sir Charles Gairdner Hospital, WA
A/Professor Eddie Lau	Radiologist	Clinical Associate Professor, Department of Radiology, Principal Fellow, Sir Peter MacCallum Department of Oncology, University of Melbourne. Head of Hybrid Imaging, Centre for Cancer Imaging, Peter MacCallum Cancer Centre, VIC
Ms Beth Ivimey	Lung cancer nurse coordinator	Prince of Wales Hospital, Randwick, NSW
Mrs Jenny Weismantel	Consumer	Consumer Representative
Ms Suzanne Bakker	Librarian	Netherlands Cancer Institute (NKI) Amsterdam, The Netherlands

Anti-Cancer Active Treatment		
A/Professor Brian McCaughan (Co-chair)	Cardiothoracic surgeon	VMO, Royal Prince Alfred Hospital, Camperdown NSW Clinical Associate Professor of Surgery, The University of Sydney, NSW
Professor Michael Boyer (Co-chair)	Medical oncologist	Clinical Professor, Central Clinical School, The University of Sydney, NSW
Dr Malcolm Feigen (Co-chair)	Radiation oncologist	Senior Consultant, Austin Hospital, Heidelberg VIC
Professor David Ball	Radiation oncologist	Professor & Chair of Lung Cancer Services, Deputy Director, Radiation Oncology & Cancer Imaging, Peter MacCallum Cancer Centre, VIC
Professor Bruce Robinson	Respiratory physician	Professor and Consultant Respiratory Physician, School of Medicine and Pharmacology Sir Charles Gairdner Hospital Unit, The University of Western Australia Scientific Director, NHMRC National

Anti-Cancer Active Treatment		
		Centre for Asbestos Related Diseases, WA
A/Professor Jenny Alison	Cardio-pulmonary physiotherapist	Associate Professor, Faculty of Health Sciences, The University of Sydney, NSW
Dr Liz Isenring	Dietitian	Clinical Academic Fellow, Princess Alexandra Hospital, Queensland Health & Conjoint Senior Lecturer in Master of Dietetic Studies Program, QLD
Ms Mary Duffy	Nurse care coordinator	Lung Cancer Services Team, Peter MacCallum Cancer Centre, VIC
Mrs Jenny Weismantel	Consumer	Consumer Representative
Mr Jeremy Cullis	Librarian	Assistant Manager/Faculty Liaison Librarian (Med Sci), The University of Sydney NSW

Palliative and Supportive Care		
Professor David Currow (Co-chair)	Palliative care specialist	Chief Cancer Officer & CEO, Cancer Institute NSW, Eveleigh NSW
A/Professor Penelope Schofield (Co-chair)	Supportive care specialist	NHMRC Research Fellow, Research Director, Department of Nursing and Supportive Care Research, Peter MacCallum Cancer Centre, VIC
Ms Beth Ivimey (Co-chair)	Lung cancer nurse coordinator	Prince of Wales Hospital, Randwick, NSW
Professor Richard M Fox		Director of Research at St Vincent's Hospital, Melbourne. VIC
Professor David Ball	Radiation oncologist	Professor & Chair of Lung Cancer Services, Deputy Director, Radiation Oncology & Cancer Imaging, Peter MacCallum Cancer Centre, VIC
Ms Kahren White	Occupational therapist	Formerly at Prince of Wales Hospital, Randwick, NSW
A/Professor Roger Goucke		Associate Professor, Department of Pain Management, Sir Charles Gairdner Hospital Clinical Associate Professor, School of Medicine and Pharmacology, The University of Western Australia, WA
A/Professor David Barnes	Respiratory physician	Clinical Associate Professor, Medicine, Central Clinical School, The University of Sydney.

		Royal Prince Alfred Hospital, NSW
Professor Geoff Mitchell	Palliative care specialist	Professor of General Practice and Palliative Care, The University of Queensland, QLD
Mrs Carol Klintfält	Consumer	Consumer Representative
Ms Yaping Liu	Librarian	Cancer Council NSW

Models of care		
A/Professor Nick Pavlakis (Co-chair)	Medical oncologist	Director of Medical Oncology, Royal North Shore Hospital, NSW Chairman of the Scientific Advisory Committee of the Australian Lung Cancer Trials Group
Ms Jocelyn Mclean (Co-chair)	Case Manager for Thoracic Surgery	Cardiothoracic Surgery, Royal Prince Alfred Hospital, Camperdown NSW
Mr Phillip Antippa	Cardiothoracic surgeon	The Royal Melbourne Hospital, VIC
Ms Kirsten Mooney	Thoracic cancer nurse coordinator	WA Cancer and Palliative Care Network, WA
Dr Peter Braude	Physician	Taree, NSW
A/Professor David Bryant	Thoracic physician	St Vincent's Hospital, Darlinghurst, NSW
Dr Roland Alvandi	Radiation oncologist	Department of Radiation Oncology, Westmead Hospital, Sydney
Mr Paul Signorelli	Consumer	Consumer Representative, Director, Doltone House, NSW
Ms Yaping Liu	Librarian	Cancer Council NSW

A.6 Potential competing interests are identified, managed and documented, and a competing interest declaration is completed by each member of the guideline development group.

Members of the Steering Committee and the five Working Groups were required to declare their potential conflict of interests in writing prior to appointment. The purpose of declaring a conflict of interest was to avoid or manage any real or perceived conflict of interest between the private interests of the Steering Committee or Working Group members (including pecuniary interest or the possibility of other advantage) and their duties as part of the Committee or Working Group – see Appendix A: **Conflict of Interest Policy**.

The members of the Steering Committee and Working Groups were required to update their information as they became aware of any changes in their circumstances. There was also an agenda item at the Steering Committee meetings where conflicts of interest was raised and documented.

All declarations of interests have been added to a register (see and have been made available to the Chair of the Steering Committee and the members of the Steering Committee. Open access to the

register allowed the Steering Committee to consider all the potential conflicts of interest during discussion, decision-making and in the formulation of the recommendations.

Table 3. Declaration of interest

Member	Declaration
Dr Andrew Penman	CEO, Cancer Council NSW, ceased employment 5th October 2012. No conflict of interest declared.
Ms Victoria Keena	Employed by Asbestos Diseases Research Institute No conflict of interest declared.
Professor Nico van Zandwijk	Member, Australasian Lung cancer Trials Group Member, American Society of Clinical Oncology Member, European Society for Medical Oncology Member, American College of Chest Physicians Member of the National Asbestos Management Review Panel (2010-2012) Other direct or indirect conflicts of interest: Presented at meetings supported by: Eli Lilly and Merck. ADRI received a research grant from Eli Lilly in 2011.
Dr Christopher Clarke	Chair, Medico-Legal BAG, Royal Australasian College of Physicians Member, CPAC, Royal Australasian College of Physicians Royal Australasian College of Physicians representative NSW MSOAP-AF. Royal Australasian College of Physicians representative Medico-legal Liaison Committee of the NSW AMA & NSW Law Society Directorship: Christopher W Clarke Pty Ltd Other direct or indirect conflicts of interest: Medico-legal reports to various bodies on asbestos related issues particularly involving patients.
Dr Henry Marshall	Employed by The Prince Charles Hospital,
Dr Steven Leong	Employed by: Queensland Health, University of Queensland, Queensland Sleep Disorders Unit.
Professor Douglas Henderson	Member: Henderson Medico legal and Consulting Member: Comcare Asbestos Innovation Fund Member: International Mesothelioma Panel Director: Henderson Medico legal and Consulting Other direct or indirect conflicts of interest: Have prepared medico legal reports on diagnosis and causation of asbestos disease for the courts in Australia and (rarely) to UK.
Professor AW (Bill) Musk	Chair: WA Mesothelioma Registry Committee Board Chairman: Busselton Population Medical Research Institute
Professor Kwun Fong	Member: Australian Lung Foundation, Lung Cancer Consultative Group Member: Cancer Australia Member: National Lung Cancer Program Director: Pulmonary Malignancy Unit (Clinical Manager) The Prince Charles Hospital, University of Queensland, Thoracic Research Centre
Professor Anna Nowak	Member: International Association for the Study of Lung Cancer, Mesothelioma Staging Committee Member: International Association for the Study of Lung Cancer, World Conference on Lung Cancer, Local Organising Committee Other direct or indirect conflicts of interest: Travel funding from Eli Lilly Australia
Dr Robert Loneragan	Employer: NSW Health Member: Chairman, NSW Branch Committee of Royal Australian and New Zealand College Radiologists (Honorary) no conflict of interest declared.
A/Professor Brian McCaughan	Employer: Self- employed, Other Institutions: Royal Prince Alfred Hospital, Strathfield Private Hospital Chair, Board Clinical Excellence Commission NSW Chair, Board Agency for Clinical Innovation NSW Other direct or indirect conflicts of interest: I treat many patients with mesothelioma and in selected cases recommend surgery.
Professor Michael Boyer	Employer: Sydney Local Health District, Lifehouse at Royal Prince Alfred Hospital

	Directorship: Lifehouse at RPA; Directorship: International Association for the Study of Lung Cancer. Other director or indirect conflicts of interest: Honoraria/travel support from: Eli Lilly, Roche Products, Boehringer Ingelheim, Pfizer, Amgen
Dr Malcolm Feigen	No conflict of interest declared.
Professor David Currow	Employer: Cancer Institute NSW & Flinders University
A/Professor Penelope Schofield	Employer: Peter MacCallum Cancer Centre, Cancer Council of Victoria, Cancer Institute of NSW. Member: Associate Editor, Journal of Supportive Care in Cancer Member: NHMRC GRP Other direct or indirect conflicts of interest: Lead author on Communication Guidelines Published research on psychosocial issues. Quality of Life and complementary medicine in cancer.
Ms Beth Ivimey	No conflict of interest declared.
A/Professor Nick Pavlakis	Employer: RNSH, Armidale Oncology Day Centre Member: Lung Cancer Advisory boards: Eli Lilly, Roche, Pfizer, Astra Zeneca, Boehringer Ingelheim Directorships: Northern Cancer Institute
Ms Jocelyn McLean	Employer: Sydney Local Health District, RPAH, Strathfield Private Hospital. Member: NSW OG – Lung – Committee Member ANZ Lung Cancer Nurses Forum
Ms Suzanne Bakker	Employer: Netherlands Cancer Inst. / Antoni van Leeuwenhoek Hospital
Mr Jeremy Cullis	Employer: University of Sydney No conflict of interest declared.
Ms Yaping Liu	No conflict of interest declared.
Mr Paul Signorelli	Director: Doltone House Director: Biaggio Signorelli Foundation
Mrs Carol Klintfält	No conflict of interest declared.
Mrs Jenny Weismantel	No conflict of interest declared.
Mr Morgan Windsor	No conflict of interest declared.
Dr Richard Slaughter	No conflict of interest declared.
Dr Annabelle Mahar	No conflict of interest declared.
Dr Belinda Clarke	No conflict of interest declared.
Dr Amanda Segal	Employer: PathWest, Health Department of WA
A/Prof Roslyn Frances	Employer: University of Western Australia / Sir Charles Gardner Hospital, Royal Perth Hospital (occasional locum). Member: Australia and New Zealand Society of Nuclear Medicine (WA Branch) Committee Member
A/Professor John Alvarez	No conflict of interest declared.
A/Professor Eddie Lau	Employer: Peter MacCallum Cancer Centre, University of Melbourne
Professor David Ball	Employer: Peter MacCallum Cancer Centre, Royal Melbourne Hospital Other direct or indirect conflicts of interest: Advisory Boards: Lilly oncology, Pfizer, Astra-Zeneca, Boehringer Ingelheim.
Professor Bruce Robinson	Employer: University of WA, Dept of Health, WA No conflict of interest declared.
A/Professor Jenny Alison	Employer: The University of Sydney Other: Royal Prince Alfred Hospital, Sydney Local Health District. Member, Australian Lung Foundation, COPD Committee, NSW Agency for Clinical Innovation, Respiratory Network
Dr Liz Isenring	Employer: Princess Aldexandra Hospital & University of Queensland Member: Associate Editor Nutrition & dietetics, Editor of Nutrition Section, Current Oncology.
Ms Mary Duffy	No conflict of interest declared.
Professor Richard Fox	Employer: Research Directorate, St Vincents Hospital Melbourne, Medico-legal reports re patient with mesothelioma for law officer/ Insurance Company. Member: Cancer Council Victoria, Grants committee of Cancer Institute

	NSW. Directorship: Member, Direct Manufacturing Centre (CSIRO) Board Melbourne & Force Industries (Victoria).
Ms Kahren White	Employer: South East Sydney Local Health District. Small private medico-legal occupational therapy practice. Occupational Therapy Australia NSW Division. Member: NSW Oncology Group for Lung Cancer – NSW Cancer Institute
A/Professor Roger Goucke	Employer: Sir Charles Gairdner Hospital, Private Practice Member: Mundiphasma, Jensen Glag
A/Professor David Barnes	Employer: Self employed respiratory Physician VMO in respiratory medicine, Royal Prince Alfred Hospital. Member: National Lung Cancer Advisory Group, Cancer Australia
Professor Geoff Mitchell	Employer: University of Queensland, Limestone Medical Centre. Member: Ipswich & West Moreton Local Medical Association
Mr Philliup Antippa	Employer: Royal Melbourne Hospital, Peter MacCallum Cancer Centre Member: Victorian Comprehensive Cancer Centre – Clinical Working group. Vice President, Senior Medical Staff – RMH Other direct or indirect COI: Member: Johnston & Johnston Ethical Endoscopy Thoracic Advisory Board Member: Astra-Zeneca Advisory Board.
Ms Kirsten Mooney	Employer: WACPCN – WA Cancer & Palliative Care Network. Member: Australia & New Zealand Lung Cancer Nurses Forum.
Dr Peter Braude	No conflict of interest declared.
A/Professor David Bryant	No conflict of interest declared.
Dr Roland Alvandi	No conflict of interest declared.

A.7 A list of organisations formally endorsing the guideline is provided.

These guidelines will be submitted to the National Health and Medical Research Council of Australia for consideration of approval.

A.2.1 The amount and percentage of total funding received from each funding source is stated.

The development of these Guidelines was funded by:

Funding Source	**Amount**	**Percentage**
Biaggio Signorelli Foundation -donation	$125,000	31%
Cancer Institute of NSW - grant	$10,000	2%
Cancer Council NSW- contribution	$25,000	6%
Asbestos Diseases Research Institute - In-kind contributors of over 2,000 hours	$206,540	51%

Publication of these Guidelines was funded by:

Comcare, Asbestos Innovation Fund - grant	$40,000	10%

A.4.1 The guideline development process includes participation by representatives of Aboriginal and Torres Strait Islander peoples and culturally and linguistically diverse communities (as appropriate to the clinical need and context), and the processes employed to recruit, involve and support these participants are described.

The mining and the intensive use of asbestos, and its products in the previous century, has had a tragic consequence for Australia as it is now one of the countries with the highest incidence of malignant mesothelioma in the world. Asbestos mining, milling and transport also affected some

aboriginal communities, notably those of Wittenoom, Roebourne and Baryulgil (2, 3). Unfortunately there is little systematic information available on the burden of disease affecting these communities. The frequency of malignant pleural mesothelioma is low and survival short, so it is unsurprising that, despite the close engagement of groups affected by asbestos, no Aboriginal consumer representatives were identified. To date, data on the incidence of mesothelioma and mortality in Aboriginal and Torres Strait Peoples or any other culturally and linguistically diverse group has not been reliably estimable due to inadequate recording. However, since the 1st July 2010 all new cases of mesothelioma diagnosed in Australia is being monitored by the Australian Mesothelioma Registry. At this stage there are limitations with reporting of trends and projections due to the lack of data. Although research is needed to close this gap these Guidelines do not specifically deal with the epidemiology of malignant mesothelioma, population measures to reduce exposure risk, screening and early detection, chemoprevention or other personalised prevention measures in exposed individuals, including Aboriginal and Torres Strait Islander peoples or any other groups.

These Guidelines will focus on the clinical pathway when a person presents with signs and symptoms, and/or preliminary tests, suggestive of malignant pleural mesothelioma. The recommendations made will be relevant for all Australians, whether in remote or urban areas, including Aboriginal and Torres Strait Islander peoples or any other groups.

D. Guideline recommendations

Table 4. Summary of recommendations

Chapter 2

Recommendations		Grade
1.	CT-guided core biopsy or VAT-guided pleural biopsy is recommended – depending on the clinical circumstances – to obtain adequate tissue for histological analysis including immunohistochemistry, and has high sensitivity and specificity for the diagnosis of malignant pleural mesothelioma.	A
2.	Cytological recognition of an atypical mesothelial proliferation in pleural effusion fluid from patients may be sufficient for diagnosis in some patients when correlated with the clinical background and imaging studies, and when biopsy is considered inadvisable or unnecessary.	C
3.	It should be standard *histopathological* practice to subtype mesotheliomas into epithelial (epithelioid), sarcomatoid and biphasic types (and other rare variants) and the distinction between epithelial versus sarcomatoid mesothelioma carries prognostic significance.	B
4.	A panel of immunohistochemical markers should be used for pathologic diagnosis of malignant pleural mesothelioma.	B
5.	The immunohistochemical panels should contain positive (mesothelial) and negative (carcinoma-related) markers for malignant mesotheliomas with an epithelioid component and include at least one cytokeratin marker, at least two mesothelial markers and at least two carcinoma-related markers.	B
6.	For pleural mesothelioma-like tumours with an epithelial component, it is recommended that immunolabelling for both calretinin and TTF-1 is routinely carried out.	B
7.	Additional markers should be added when tumours other than lung cancer enter into the differential diagnosis.	B
8.	The immunoprofile of sarcomatoid mesotheliomas including desmoplastic mesothelioma is more restricted than that for mesotheliomas with an epithelial component, with variable expression of markers such as cytokeratin 5/6, calretinin, WT1 and podoplanin (D2-40). Labelling for cytokeratins is important and can facilitate assessment of invasion. However, cytokeratin-negative sarcomatoid mesotheliomas are recognised.	B
9.	Tissue invasion should be demonstrated by histology or imaging studies to diagnose malignant mesothelioma definitively.	B
10.	Measurement of the blood SMRP level is not recommended for routine clinical diagnosis.	B

Chapter 3

Recommendations		Grade
11.	The TNM system should be used for disease staging in mesothelioma.	B
12.	Patients with suspected or confirmed malignant pleural mesothelioma diagnosis should be assessed for therapeutic planning with CT of the thorax and abdomen with contrast enhancement.	A
13.	CT or ultrasonography should be used to guide biopsy and drainage of pleural effusion.	B
14.	FDG-PET is a more sensitive modality than CT to detect possible lymph node involvement and distant metastatic disease, and should be performed when the presence of disease in these sites will influence a management plan.	A
15.	FDG-PET-CT should be used in preference to FDG-PET where available.	A
16.	MRI should not be part of a routine assessment of patients with mesothelioma.	B
17.	MRI with gadolinium enhancement can be useful in specialised situations where it is important to delineate tumour extension in the diaphragm, endothoracic fascia, chest wall or through iatrogenic tumour seeding.	C
Consensus based recommendation		
i.	Routine mediastinoscopy and other invasive procedures are not indicated in patients receiving supportive care or palliative management with chemotherapy.	
18.	Mediastinoscopy is recommended as an additional staging procedure for patients being considered for radical surgery in order to exclude N2 level nodal disease or to confirm pathological involvement where imaging is equivocal.	B
19.	The addition of EUS-FNA and or EBUS is feasible in mesothelioma and may identify additional N2, T4, and M1 disease.	C
20.	Bilateral thoracoscopy and laparoscopy with peritoneal lavage may identify additional M1 disease or sarcomatoid histology and taking the potential morbidity associated with radical surgery into account extended (surgical) staging should be considered for all patients with malignant pleural mesothelioma before resection.	B
21.	Baseline prognostic assessment should include evaluation of important patient, clinical, biological and imaging factors.	
a.	Epithelioid histological type and performance status ≤ 1 are relatively favourable prognostic factors.	A
b.	Male sex, weight loss and chest pain are unfavourable prognostic factors.	B
c.	Elevated white cell count is an unfavourable prognostic factor.	B

Recommendations		Grade
d.	Other markers of inflammation also confer an unfavourable prognosis.	C
e.	Measurement of either SUV max or TGV by FDG-PET provides prognostic information in patients with MPM.	C
22.	During treatment:	
a.	Assessment of treatment response using quantitative FDG-PET parameters is predictive of survival outcome.	B
b.	Nodal stage ≤ 1, minimal residual disease and epithelioid histology are favourable prognostic factors.	A
c.	Increasing serum SMRP levels during treatment are an unfavourable prognostic marker.	B
23.	Following suspected recurrence:	
a.	FDG-PET-CT should be performed when a diagnosis of recurrence after previous radical surgical therapy is equivocal on other imaging modalities.	B
b.	Measurement of SUVmax on FDG-PET-CT following post-surgical relapse is predictive of survival outcome.	C
24.	Pleurodesis status should be known when interpreting results of CT or FDG–PET imaging.	B
25.	The extent of pre-treatment evaluation, including radiological evaluation and assessment of clinical and laboratory prognostic factors should be considered in the context of potential and appropriate management options.	C C
26.	In patients being considered for radical treatment, assessment should include pulmonary and cardiac function testing and evaluation of psychological status and comorbidities.	C
27.	Pre-treatment evaluation of patients considered for chemotherapy should include assessment of comorbidities and general fitness.	

Chapter 4

Recommendation		Grade
28.	Combination chemotherapy (pemetrexed and cisplatin or carboplatin) should be used in first-line treatment rather than single drug treatment.	A
Consensus based recommendation		
ii.	Immunologically based and targeted therapies for patients with malignant mesothelioma should be restricted to clinical trials.	
29.	Thoracoscopic pleurodesis is an effective treatment option to control recurrent malignant pleural effusions in mesothelioma.	B
30.	If the thoracoscopic pleurodesis is not appropriate or fails, palliative pleurectomy/decortication should be considered for symptom control.	C
31.	Only patients with favourable prognostic features, and favourable histology and staging, should be referred for consideration of radical treatment involving extensive	A

Recommendation		Grade
	cytoreductive surgery.	
32.	Radical surgical approaches should be restricted to institutions with significant surgical experience and high volume of cases.	B
33.	Extensive cytoreductive surgery should only be used as part of multimodality treatment.	B
34.	Mesothelioma is sensitive to moderately high radiation doses and radiotherapy is advocated for palliation of symptomatic tumour masses arising from the pleural cavity or metastases in other locations.	C
35.	For doses greater than 50 Gy, advanced radiotherapy technologies with strict constraints for contralateral lung doses are recommended to avoid excessive toxicity.	C
36.	The administration of prophylactic radiotherapy following pleural interventions in patients with mesothelioma has no effect on changing the disease course and is not recommended.	C

Chapter 5

Recommendations		Grade
37.	Pleurodesis should be used to prevent recurrent pleural effusions.	B
38.	Regular oral low dose, sustained release opioids should be given to reduce the intensity of breathlessness.	B

Clinical practice points	
a:	VAT is not only the gold standard for securing biopsy tissue for the pathological diagnosis, but it also allows effective drainage of pleural effusion and talc pleurodesis.
b:	It is recommended that – unless loculation of the fluid or other physical constraints prevent adequate sampling of the effusion fluid – a minimum of 100 ml of effusion fluid and preferably the entire volume of fluid is submitted for cytology (after sampling of small volumes for biochemical and microbiological assessment). Such sampling is advocated to allow recovery of sufficient numbers of cells for cell block sections and immunohistochemical studies.
c:	The anatomical site and extent of lesions should be determined.
d:	When tissue invasion cannot be identified, the lesion should be designated as an atypical mesothelial proliferation.
e:	New-generation spiral CT should be used in imaging malignant pleural mesothelioma.
f:	A multidisciplinary team with sufficient experience should provide advice on the suitability of patients for trimodality therapy and the ongoing treatment strategy adopted.
g:	Patients whose MPM progresses despite induction (neoadjuvant) chemotherapy

Clinical practice points	
	should not be offered cytoreductive surgery followed by hemithoracic radiotherapy.
h:	Patients with malignant mesothelioma should be referred to a palliative care specialist in a timely manner, and on the basis of their needs.
i:	The WHO principles of cancer pain management for patients with malignant mesothelioma should be followed.
j:	A specialist palliative care physician should be involved early as part of the multidisciplinary oncology team for patients with refractory or unresponsive pain.
k:	Palliative radiotherapy should be considered for patients with painful chest wall infiltration or nodules.
l:	In order to tailor information to a person's individual needs at a particular point in time, it is necessary to: ▪ give clear information specific to the individual ▪ repeat and summarise important information ▪ encourage questions ▪ actively check the person's understanding, and ▪ provide additional written/audiovisual information.
m:	Patients should be screened for psychological distress and unmet needs.
n:	Patients and carers should be referred to appropriate counseling services when required.
o:	Information, guidance and emotional support should be provided for carers.
p:	Consultations should be provided with specialist nurses trained in the care of patients with malignant pleural mesothelioma.
q:	A multidisciplinary team approach will ensure consistency in patient management through the development of a multidisciplinary care plan that will guide patient treatment throughout their illness and provide support for their carers.
r:	Treating specialists and/or the MDT should establish communication with the patient's GP as soon as possible after diagnosis, and keep them informed about their patient's changing needs and whom they should contact for expert advice.
s:	Nurse care coordinators are important members of the MDT. They provide support and information to patients with mesothelioma, ensure timely and appropriate referrals, help navigate the patient through their disease journey and coordinate their multidisciplinary care.
t:	Where mesothelioma-specific treatment options, including surgery, are not available in a given centre, medical teams should refer patients to centres offering expert mesothelioma care for discussion of all potential treatment options and care planning.
u:	The frequency and type of follow-up should be determined by individual patient symptoms, the stage of the disease and the treatment goals. CT scanning is the most useful investigation for evaluating disease progress.
v:	Allied health professionals are important members of the MDT and contribute to symptom management and improved quality of life in patients with malignant mesothelioma.

D.6 The method used to arrive at consensus-based recommendations or practice points (Requirements D.4 and D.5) (e.g. voting or formal methods, such as Delphi) is documented.

These guidelines will include evidence-based recommendations, consensus-based recommendations and practice points as defined below.

1. Evidence-based recommendation is a recommendation formulated following a systematic review of the evidence and with supporting references. (Sufficient evidence)
2. Consensus-based recommendation is a recommendation formulated in the absence of quality evidence, or low quality evidence, as the result of a systematic review of the evidence failing to identify acceptable/admissible evidence on the clinical question. (Insufficient evidence (low quality)
3. Practice point is a recommendation to provide additional information to support recommendations where a systematic evidence review was not conducted and are based on expert opinion and formulated through a consensus process. (Clinical practice points where no, or only a low level of evidence was available.)

The guidelines have been by the co-chairs of each Working Group. Concurrently the evidence in the literature has been reviewed and graded by an expert team according to NHMRC guidelines. Where there the first and second readers disagreed on either study type or level of evidence, a third reader independently re-assessed the article. It two out of three readers agreed, consensus had been achieved, if not, the paper was tabled for review at an open consensus meeting by three of the readers and consensus achieved through discussion - see Technical Report; C.5. Study Selection; p53-90.

D.15 The guideline and recommendations have been assessed by at least two reviewers, independent of the guideline development process, using the AGREE II instrument.[3, 5]

The guidelines and recommendations have been assessed by two independent reviewers using the AGREE II instrument (4) see Appendix B.

F. Public consultation

F.1 The process for public consultation on the draft guideline complies with Section 14A of the Commonwealth *National Health and Medical Research Council Act 1992*1 and accompanying regulations.

As part of the public consultation process the following advertisement appeared in The Australian on the 21st January 2013.

Asbestos Diseases Research Institute

Draft Guidelines for the Diagnosis and Treatment of Malignant Pleural Mesothelioma

Proposed for submission to the NHMRC for approval under section 14A of the *National Health and Medical Research Council Act 1992*.

The Asbestos Diseases Research Institute has prepared draft Guidelines on the Diagnosis and Treatment of Malignant Pleural Mesothelioma

You are invited to make a submission to Asbestos Diseases Research Institute on the draft guidelines.

How to make a submission

You may make a submission in writing. Please send it to:

Asbestos Diseases Research Institute

PO Box 3628

Rhodes NSW 2138

Please include your name, address or telephone number at which you can be contacted.

Closing date: Friday 22nd February 2013

Your submission must be received at the above address by 25th February 2013.

Further information

A copy of the draft guidelines can be obtained from: www.adri.org.au

or by contacting: 02 97679800

F3. During the public consultation period, the developer has undertaken and documented consultation with: – the Director-General, Chief Executive or Secretary of each state, territory and Commonwealth health department

For public consultation the Guidelines were sent to following state, territory and Commonwealth health departments for comment.

Commonwealth

The Hon Tanya Plibersek MP - Minister for Health
PO Box 6022
House of Representatives
Parliament House
Canberra ACT 2600

Ms Jane Halton
Secretary
Department of Health and Ageing
GPO Box 9848,
Canberra ACT 2601, Australia

Professor Chris Baggoley
Chief Medical Officer
Department of Health and Ageing
GPO Box 9848,
Canberra ACT 2601, Australia

ACT
Ms Katy Gallagher MLA
Minister for Health
Minister for Women
Minister for Children and Young People
PO Box 1020
CANBERRA ACT 2601

Dr Peggy Brown
Chief Executive
ACT Health
GPO Box 825
CANBERRA ACT 2601

NSW
The Hon. Jillian Skinner, MP
Minister for Health, and Minister for Medical Research
The Hon. Jillian Skinner, MP
Level 31 Governor Macquarie Tower
1 Farrer Place
SYDNEY NSW 2000

Dr Mary Foley
Director-General
Ministry of Health
NSW Health
Locked Mail Bag 961

North Sydney NSW 2059
Australia

QLD
The Hon Lawrence Springborg MP
Minister for Health
GPO Box 48
BRISBANE QLD 4001

Dr Tony O'Connell
Director-General
Queensland Health
GPO Box 48 Brisbane, Qld 4001

VIC
The Hon David Davis MP
Minister for Health
GPO Box 4057
Melbourne VIC 3001

Dr Pradeep Philip
Secretary
Department of Health (Victoria)
GPO Box 4541
Melbourne VIC 3001

SA
The Hon John Hill MP
Minister for Health and Ageing
GPO Box 2555
Adelaide SA 5001

Mr David Swan
Chief Executive
Department for Health and Ageing
PO Box 287
Rundle Mall SA 5000

WA
The Hon Dr Kim Hames MLA
Minister for Health
28th Floor, Governor Stirling Tower
197 St Georges Terrace
Perth WA 6000

Mr Kim Snowball
Director General
WA Department of Health
PO Box 8172
Perth Business Centre WA 6849

NT
The Hon David Tollner MLA
Minister for Health
GPO Box 3146
Darwin NT 0801

Mr Jeff Moffet
Chief Executive
Department of Health & Families
GPO Box 40596
Casuarina NT 0811

TAS
The Hon Michelle O'Byrne MP (Chair)
Minister for Health
GPO Box 1470
Hobart TAS 7001

Mr Matthew Daly
Secretary
Department of Health
GPO Box 125B
Hobart TAS 7001

F.4The developer has identified and consulted with key professional organisations (such as specialty colleges) and consumer organisations that will be involved in, or affected by, the implementation of the clinical recommendations of the guideline.

Australasian Lung cancer Trials Group (ALTG)
Associate Professor Paul Mitchell ALTG President
The Australian Lung Foundation
PO Box 847
Lutwyche, QLD 4030

Australian Lung Foundation (ALF)
The Australian Lung Foundation
PO Box 847
Lutwyche, QLD 4030

Australian Manufactures Workers Union (AMWU)
Paul Bastian - National Secretary
Australian Manufacturing Workers Union
Unions NSW
AMWU Building, Level 2
133 Parramatta Road
Granville NSW 2142

Asbestos Diseases Foundation of Australia (ADFA)
Mr Barry Robson
President – ADFA
Suite 3, Ground Floor
133-137 Parramatta Road
Granville NSW 2142

Asbestos Injuries Compensation Fund
Narreda Grimley
General Manager
Asbestos Injuries Compensation Fund Limited
Suite 1, Level 7, 233 Castlereagh Street
Sydney NSW 2000

Biaggio Signorelli Foundation
Paul Signorelli
Pier 19-21 Upperdeck
26-32 Pirrama Road,
Pyrmont NSW 2009

Cancer Australia
Dr Helen Zorbas - CEO
Locked Bag 3,
STRAWBERRY HILLS NSW 2012

Cancer Council Australia
Professor Ian Olver – CEO
Cancer Council Australia
GPO Box 4708,
Sydney NSW 2001

Cancer Institute NSW
Professor David Currow – CEO
Level 9, 8 Central Avenue
Australian Technology Park
Eveleigh NSW 2015

Cancer Voices Australia
http://www.cancervoicesaustralia.org/
E: info@cancervoicesaustralia.org
P: 0415 785 814

Clinical Oncological Society of Australia (*COSA)*
GPO Box 4708
Sydney NSW 2001
cosa@cancer.org.au

Department of Health and Ageing (DOHA)
Prof Chris Baggoley
Chief Medical Officer
GPO Box 9848,
Canberra ACT 2601, Australia

Dust Diseases Board of NSW (DDB)
Ms Anita Anderson
Level 2
82 Elizabeth Street
Sydney NSW 2000
enquiries@ddb.nsw.gov.au

Dust Diseases Tribunal
Chairman
Locked Bag 16
HAYMARKET
NSW 1240

Palliative Care Australia
PO Box 487
Strawberry Hills NSW 2012
info@palliativecarensw.org.au

Royal Australian College of General Practitioners (RACGP)
RACGP College House
100 Wellington Parade
EAST MELBOURNE VIC 3002
racgp@racgp.org.au

Royal Australian College of Physicians (RACP)
145 Macquarie Street
SYDNEY NSW 2000
racp@racp.edu.au

Royal Australian College of Surgeons (RACS)
Royal Australasian College of Surgeons
College of Surgeons' Gardens
250-290 Spring Street
East Melbourne VIC 3002 Australia
college.sec@surgeons.org

Thoracic Society of Australia and New Zealand (TSANZ)
GPO Box 1491
SYDNEY NSW 2001
info@thoracic.com.au

Therapeutic Goods Administration (TGA)
TGA
PO Box 100
Woden ACT 2606 Australia
info@tga.gov.au

Pharmaceutical Benefits Advisory Committee (PBAC)
GPO Box 9848,
Canberra ACT 2601, Australia

Medical Services Advisory Committee (MSAC)
MSAC Secretariat through HTA Access Point
Australian Government Department of Health and Ageing
MDP 851
GPO Box 9848
CANBERRA ACT 2601
Email:hta@health.gov.au

Table 5. F.2.1 A version of the public consultation submissions summary is publicly available, with submissions de-identified.

Guidelines for the Diagnosis and Treatment of Malignant Pleural Mesothelioma
Public Consultation – Submissions

The draft Guidelines for the Diagnosis and Treatment of Malignant Pleural Mesothelioma were open for Public Consultation from the 21st January 2013 to the 22nd February 2013 as advertised in The Australian on Monday 21st January 2013.

	COMMENTER (de-identified)	**COMMENTS**	**GUIDELINES**	**AMENDMENTS**
1	A Director of a Government Health Department	Page 6 and Page 22 MPM guidelines suggest that a third, non-occupational wave of mesothelioma cases has developed and that these patients are likely to be end users of asbestos products. This assertion is questionable and based on a single methodologically flawed reference. The changing epidemiological profile of asbestos related diseases is of considerable interest and requires ongoing study. However, based on current evidence, it is premature to suggest there is a 'third wave'. Methodological issues of concern are outlined below by critical appraisal of the cited paper. Critical Appraisal of the Olsen et al paper (MJA 2011; 195 (5):271-4	**Executive Summary** **Page 8** Although the current epidemic of malignant mesothelioma is closely associated with past occupational exposure there is increasing evidence that a third, non-occupational wave of mesothelioma cases has developed.	**Executive Summary** **Page 8** Although the current epidemic of malignant mesothelioma is closely associated with past occupational exposure there is data that suggests a third, non-occupational wave of mesothelioma cases is developing, which underlines the importance of strengthening counter-measures to avoid non-occupational exposure.
			Introduction **1.2 History of mesothelioma** **Page 24** Now, patients are more likely to be end-users, who have been exposed when installing products containing asbestos, doing home renovations or handling materials containing asbestos that remain in older buildings and structures (5).	**Introduction** **1.2 History of mesothelioma** **Page 24** People with mesothelioma are increasingly likely to be end-users, who have been exposed when installing products containing asbestos, doing home renovations or handling materials containing asbestos that remain in older buildings and structures (5).

	COMMENTER (de-identified)	COMMENTS	GUIDELINES	AMENDMENTS
			1.3 Incidence of malignant mesothelioma **Pages 25-26** Most deaths caused by malignant mesothelioma should be preventable. Although the current epidemic of malignant mesothelioma is closely associated with past occupational exposure, there is increasing evidence that a third, non-occupational wave of mesothelioma cases has developed (5). Primary prevention is vitally important and requires experts in occupational hygiene, epidemiologists and other specialists to address this significant problem – the large amounts of asbestos present in the Australian environment – which has the potential to cause further deaths.	**1.3 Incidence of malignant mesothelioma** **Pages 25-26** Most deaths caused by malignant mesothelioma should be preventable. Although the current epidemic of malignant mesothelioma is closely associated with past occupational exposure, a recent study suggests that a third, non-occupational wave of mesothelioma cases has developed (5). The frequency of cases attributable to occupational exposure may have begun to decline owing to stringent control of occupational exposure. However, the frequency of cases with a non-occupational exposure history does not seem to have declined. Data suggests that among this group the proportion attributable to home renovation has been increasing and may now account for a majority of documented non-occupational exposure (6). Case-controlled studies are needed to verify these findings. Given the widespread presence of asbestos in the built environment and the potential exposure in less controlled settings, stronger counter-measures to strengthen exposure control in the domestic setting are needed. Primary prevention is vitally important and requires experts in occupational hygiene, epidemiologists and other specialists to address this significant problem – the large amounts of asbestos present in the Australian environment – which has the potential to cause additional cases of asbestos-related diseases.
2	A Health Officer, Government Health Department	...the statements on page 6 and page 23 of the draft guidelines referring to a postulated third wave of non-occupational mesothelioma cases be removed, given that the case series published and quoted on the area (Olsen et al, MJA 2011)	As above	As above
3	A radiation oncologist	4.6.3 Prophylactic radiotherapy I think that the present evidence supports something along the lines of... Although evidence is conflicting, it is likely that	**4.6.3 Prophylactic radiotherapy** **Pages 90-91** Two systematic reviews of three randomised and nine non-randomised trials concluded that treatment of subcutaneous nodules with prophylactic radiotherapy was not justified and had	**4.6.3 Prophylactic radiotherapy** **Pages 90-91** Two systematic reviews of three randomised and nine non-randomised trials concluded that the use of prophylactic radiotherapy in thoracic intervention sites to prevent

	COMMENTER (de-identified)	COMMENTS	GUIDELINES	AMENDMENTS
		prophylactic radiotherapy following simple pleural interventions carries little clinical benefit and can be safely avoided. In the setting of more invasive interventions, there is inadequate high level data to provide definitive recommendations. "radiotherapy does not alter the disease course in a clinically significant way"	no significant effect on overall survival (7, 8). However, the three randomised studies were underpowered and showed variations in the timing, dose/portal, fractionation of radiotherapy and follow-up (9-11). **Recommendation 36** **Pages 91** The administration of prophylactic radiotherapy following pleural interventions in patients with mesothelioma has no effect on changing the disease course and is not recommended.	subcutaneous nodules was not justified and had no significant effect on overall survival (7, 8). The three randomised studies were underpowered and showed variations in the timing, dose/field size, fractionation of radiotherapy and follow-up (9-11). The weight of evidence does not support a local control benefit of prophylactic radiotherapy following simple thoracic intervention that justifies its use. **Recommendation 36** **Pages 91** The administration of prophylactic radiotherapy following pleural interventions in patients with mesothelioma has no significant effect on changing the disease course and is not recommended.
4	From a pharmaceutical company	Recommendation 28: Combination chemotherapy (pemetrexed and cisplatin or carboplatin) should be used in first-line treatment rather than single drug treatment). Please clarify what is meant by: 'providing indirect evidence that combination treatment has a beneficial effect" within the context of the summary. Updated survival figures have not been included see: Vogelzang et al Long-term survival update from the randomized phase 111 study of pemetrexed plus cisplatin vs cisplatin in patients with malignant pleural mesothelioma (MPM). Lung Cancer 2005:49:S230.	**4.2.1 Combination chemotherapy** **Pages 77-78** Two randomised studies have shown that combination chemotherapy that includes cisplatin and pemetrexed or raltitrexed is associated with increased survival (12, 13). The median overall survival of patients given cisplatin–pemetrexed (12.1 months) or cisplatin–raltitrexed (11.4 months) was significantly longer than that of patients receiving cisplatin alone (9.3 and 8.8 months respectively), providing indirect evidence that combination treatment has a beneficial effect. A large compassionate-use study of cisplatin or carboplatin in combination with pemetrexed suggests that carboplatin and cisplatin have similar efficacy (14). **Recommendation 28** **Page 78** Combination chemotherapy (pemetrexed and cisplatin or carboplatin) should be used in first-line treatment rather than single drug treatment. **Suggested reference**	**4.2.1 Combination chemotherapy** **Pages 77-78** Two randomised studies have shown that combination chemotherapy that includes cisplatin and pemetrexed or raltitrexed is associated with increased survival (12, 13). The median overall survival of patients given cisplatin–pemetrexed (12.1 months) or cisplatin–raltitrexed (11.4 months) was significantly longer than that of patients receiving cisplatin alone (9.3 and 8.8 months respectively), providing direct evidence that this combination treatment has a beneficial effect. A large compassionate-use study of cisplatin or carboplatin in combination with pemetrexed suggests indirectly that carboplatin and cisplatin have similar efficacy (14). **Recommendation 28** **Pages 78** Combination chemotherapy (pemetrexed and cisplatin or carboplatin) rather than single drug treatment should be used as first-line systemic treatment for malignant pleural mesothelioma. **Comment:** The abstract by Vogelzang was not included as it was outside the inclusion criteria.

	COMMENTER (de-identified)	COMMENTS	GUIDELINES	AMENDMENTS
5	Laywers	5.9 Legal compensation issues a. Compensation cases for mesothelioma are not limited to circumstances in which the mesothelioma has arisen.... b. The process of making a claim for mesothelioma differs between States.... c. Doctors and health care providers can play a role in minimizing the potential stress of legal claims... d. ..supports the provision of psychosocial support to people diagnosed with mesothelioma including those with legal claims...	**5.9 Legal compensation issues** **Page 106** Because malignant mesothelioma frequently results from occupational exposure to asbestos, patients whose work involved dealing with asbestos may be eligible for legal compensation. Compensation claims frequently occur while the patient and family members are trying to deal with the diagnosis and treatment of an incurable disease and to cope with progressive symptoms and impending death. **Page 106** It is important to be aware that patients who have occupationally acquired malignant mesothelioma may be experiencing additional stress related to legal processes. These patients and families may require additional psychosocial support.	**5.9 Legal compensation issues** **Page 106** Because malignant mesothelioma frequently results from exposure to asbestos, patients who have a history of exposure to asbestos may be eligible for legal compensation. Compensation claims frequently occur while the patient and family members are trying to deal with the diagnosis and treatment of an incurable disease and to cope with progressive symptoms and impending death. The avenues for compensation vary between States. **Page 106** It is important to be aware that patients who have malignant mesothelioma may be experiencing additional stress related to legal processes. These patients and families may require additional psychosocial support. ..... Note: The evidence provided is grounded in the references sited and not opinion only.
6	Laywers	5.9 Legal compensation issues “”provides an inaccurate reflection of the legal situation in Australia and the experience of the legal process by the majority of MM sufferers. ..... should be amended to reflect a balanced view of the legal process and experiences of MM sufferers in Australia.’ .... It is our strong opinion that MM sufferers should, at the very least, be advised (in a general sense) that they have legal rights and to seek professional legal assistance....	**5.9 Legal compensation issues** **Page 106** Because malignant mesothelioma frequently results from occupational exposure to asbestos, patients whose work involved dealing with asbestos may be eligible for legal compensation. Compensation claims frequently occur while the patient and family members are trying to deal with the diagnosis and treatment of an incurable disease and to cope with progressive symptoms and impending death. ..... Suggested **Recommendation** “Sufferers of MM should be advised that they have legal rights to claim statutory entitlements and common law compensation and be advised to consult an expert lawyer when they are able to do so. This advice should be given at the time of diagnosis and shortly after and followed up with during the course of the patient’s treatment.”	**5.9 Legal compensation issues** **Page 106** Because malignant mesothelioma frequently results from exposure to asbestos, patients who have a history of exposure to asbestos may be eligible for legal compensation. Compensation claims frequently occur while the patient and family members are trying to deal with the diagnosis and treatment of an incurable disease and to cope with progressive symptoms and impending death. The avenues for compensation vary between States. **New** **Clinical Practice Point Q** **Page 107** Practitioners dealing with MPM patients should be aware that legal remedies are available and the patient should be advised of this upon diagnosis.

	COMMENTER (de-identified)	COMMENTS	GUIDELINES	AMENDMENTS
7	From a Ministry for Health	Provided the Guidelines to: the Thoracic Tumour Collaborative in the ***** Cancer and Palliative Care Network Senior Environmental Health Officer, Health Protection Group	No further comment received.	
8	Government department	...the recommendations contained in these draft clinical guidelines do not have any implications to the MBS that require appraisal or comment by MSAC, ...		
9	From a Ministry for Health and Ageing	Minister for Health and Aging, Government of ****** acknowledge receipt of the Guidelines		
10	From a Ministry for Health	The draft guidelines have been reviewed by the key Medical Oncologist that treats mesothelioma. From the perspective of medical oncology / chemotherapy treatment the organisation supports the guidelines and recommendations.		
11	State Health Minister	The multidisciplinary approach you have adopted to the development of these guidelines is a positive step towards bringing a uniform approach to the treatment of this difficult disease. …commend the staff and volunteers of the Asbestos Research Institute for their continued efforts to support those affected by asbestos diseases.		

Appendix A: Conflict of Interest Policy

DEVELOPMENT OF GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF MALIGNANT MESOTHELIOMA

CONFLICT OF INTEREST POLICY

Purpose

The aim of this policy is to outline the general standards of conduct expected of members of the Steering and Working Groups for the Development of Guidelines for the Diagnosis and Treatment of Malignant Mesothelioma in relation to pecuniary or direct interests and relationships; and provides for the avoidance and appropriate management of actual, apparent, perceived or potential conflicts of interests.

Scope

This Policy applies to all members of the Steering and Working Groups for the Development of Guidelines for the Diagnosis and Treatment of Malignant Mesothelioma.

Policy Statement

All Steering and Working Groups members are required to declare actual, apparent, perceived or potential conflicts of interests on an annual basis and if members acquire, or become aware of a conflict of interest at a time after the most recent annual declaration and before the next annual declaration is due, they must provide an ad hoc declaration of that interest as soon as possible.

In NHMRC's *'Guideline development and conflicts of interest'(15)* states that for members of working groups developing guidelines a conflict of interest may involve, but not limited to, one of the following circumstances:

> *'a) financial interests such as receipt by the prospective member or 'immediate family members' (partner and dependent children) of payments, gratuities, consultancies, honoraria, employment, grants, support for travel or accommodation, payment for meals and beverages or entertainment or educational event attendance (including registration fees) or gifts from an entity having a commercial interest in the guidelines*
>
> *b) any other direct or pecuniary interest considered relevant (for instance, having provided expert testimony on behalf of an entity with a commercial or other interest in the guidelines to be developed)*
>
> *c) relationships, including board membership, employment, stock ownership or consultancies between the prospective member or 'immediate family members' (partner and dependent children) and corporations whose products or services are related to the guideline topics or that have a commercial or other interest in the guidelines to be developed*
>
> *d) affiliations to or associations with any organisations or activities which could reasonably be perceived to be an influence due to a competing interest either for or against the issue for which a guideline is being developed*
>
> *e) institutional interests (that is, interests arising from an affiliation or association of an individual to an institution) – for example, when parties with an interest in the topic of the guideline have made gifts to the member's institution to endow chairs or fund the construction of research facilities or donate equipment to support a project in which the member is involved; or when research conducted within*

an institution could affect the value of equity that the institution holds in a company or the value of a patent that the institution licenses to a company

f) a prospective member having been involved in the development of related guidelines, standards, educational materials or fact sheets, writing of publications, delivering speeches, or engagement in public debate on the topic related to the guidelines to be developed

g) receipt of research funding by the prospective member or immediate family members from any entity that has a commercial interest in the prospective guidelines

h) any other influences which might reasonably be considered likely to affect the expert judgement of the individual, or lead to the perception by others that the judgement of the individual is compromised.'

Appendix B: Independent review of the guideline development process using the AGREE II instrument.

The guidelines and recommendations have been assessed by the following independent reviewers using the AGREE II instrument.

1. Jennifer K Peat, PhD
   Honorary Professor,
   Australian Catholic University
   Consultant Statistician
   Concord Repatriation General Hospital, NSW

2. Clinical Associate Professor Michael Vallely
   Consultant Cardiothoracic Surgeon
   Royal Prince Alfred Hospital, NSW

3. Dr Jeffrey Bowden
   Respiratory Medicine Specialist
   Respiratory Unit
   Flinders Medical Centre, SA

4. Professor Stephen Ackland
   Conjoint Professor
   Faculty of Health
   Department of Medical Oncology
   Mater Hospital
   Newcastle, NSW

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