



### Medical Services Review Board

Jan. 19, 2012

Minutes

#### Members present

Beth Baker, M.D.  
Jeffrey Bonsell, D.C.  
Lisa Hanselman, OTR/L  
Kimberly Olson – *via phone*  
Rose Hatmaker  
Greg Hynan, D.C.  
Reed Pollack  
Dan Wolfe, P.T., G.D.M.T.

#### Members absent

Michael Goertz, M.D.  
Brian Konowalchuk, M.D., M.P.H.  
Robin Peterson, P.T.  
Jody Ruppert, OTR/L  
Andrew Schmidt, M.D.  
Glenda Cartney, R.N.  
Kathi Henrickson, R.N.

#### Staff members present

Kate Berger  
Assistant Commissioner, Gary Hall  
William Lohman, M.D.  
Pamela McLaughlin

#### Visitors present

Hazmer Cassim, D.O., MAPS  
Ray Bohn, WCRA  
Dawn Carlson, Almeida, P.A.  
Cristine Almeida, Almeida, P.A.  
Heather Keenan, MAPS  
Aysel Atli, M.D., MAPS  
Natalie Haefner, WCRA  
Sherri Gonya, Medtronic  
Daniel Wulff, MNAJ  
Anne Thompson, Medtronic

#### Call to order and introductions

The meeting was called to order by Chairwoman Dr. Beth Baker. Introductions were made and a quorum was declared. Member Kimberly Olson attended by telephone.

#### Approval of the minutes/agenda

The minutes from the Oct. 13, 2011, meeting of the Medical Services Review Board (MSRB) were reviewed. All members present voted in favor of a motion to approve the minutes as presented. All members present also voted in favor of a motion to approve the agenda for the meeting.

#### Introduction of new and reappointed members

New members and reappointed members were presented.

#### Assistant commissioner announcements and update

Assistant Commissioner Gary Hall gave an update:

- a Department of Labor and Industry (DLI) study of employee satisfaction with settlement of their claims;
- data analytic proposals to control medical costs in the workers' compensation system;
- the Workers' Compensation Advisory Council activity; and
- the DLI workers' compensation summit – June 12 and 13, 2012, at Cragun's Conference Center in Brainerd, Minn. – and DLI invites ideas for topics and workshops of interest to the wide workers' compensation community.

### **Housekeeping items**

Laura Zajac presented the following documents and topics:

- a proposed records retention schedule for MSRB;
- a data categories and classification document for MSRB data; and
- appointment of a responsible authority and records management officer for MSRB.

### **All members present voted in favor of the following motions**

1. A motion to approve the proposed MSRB records retention schedule, including the recommended 20-year retention period for electronic recordings of meetings.
2. A motion to approve the proposed MSRB data categories and classification document dated January 2012.
3. A motion approving a resolution appointing the assistant commissioner of the Minnesota Department of Labor and Industry, Safety and Workers' Compensation Division, or his or her designee, as (a) the responsible authority for MSRB for purposes of data practices; and (b) the records management officer for MSRB for the purpose of records retention and destruction.

### **Possible amendment to the joint rules of procedure with the Rehabilitation Review Panel**

Laura Zajac provided an update about the status of the possible amendments in Minnesota Rules chapter 5217, including amendment of the rule providing for monthly meetings. A joint request for comment has been published in the *State Register* on Dec. 27, 2011. No comments have been received, other than a request for copies of the draft rules when they become available. Reed Pollack is the designated DLI and RRP liaison for these rules. Ideas for other amendments should be forwarded to him for discussion at the next MSRB meeting.

### **Lumbar epidural steroid injections (LESI)**

A recommendation about lumbar epidural steroid injections was postponed because language for a draft rule is not yet available.

### **Draft spinal stimulator and intrathecal drug delivery system rules**

The following previously distributed handouts were sent to MSRB members for further discussion at today's meeting:

- a report about intrathecal drug delivery systems, dated July 16, 2009;
- a report about spinal cord stimulators, dated Sept. 2, 2008;
- two tables summarizing comments received and recommendations, dated April 17, 2007, and Oct. 23, 2008;
- two tables summarizing comments received and actions taken, dated July 10, 2007, and Oct. 22, 2009; and
- draft rules, dated Oct. 22, 2009.

Dr. Bill Lohman asked whether MSRB members have any recommended changes to the draft rules. Following discussion, all members present voted in favor of the following motions.

1. The draft rules should be amended to require an evaluation by a psychologist or psychiatrist in every case a spinal cord stimulator or intrathecal drug delivery system is being considered; and

2. The draft rules should be amended to require that, once the psychological evaluation has been completed, a second confirmatory opinion be obtained from a health care provider independent from the practice of the health care provider proposing the spinal cord stimulator or intrathecal drug delivery system.

The MSRB requested that Lohman and DLI bring revised language for review at its next meeting.

#### **Spinal fusion and implants**

Bill Lohman distributed policies about lumbar fusion from Medica, HealthPartners, BlueCross BlueShield of Minnesota and the Washington state Department of Labor and Industries, and a table comparing key features of the proposals with the Minnesota workers' compensation treatment parameter rules. He asked the MSRB to discuss issues about spinal fusion surgery in workers' compensation.

- Is there a problem?
- If so, why is there a problem?
- Can anything be done to address the problem?
- Is the number of surgeries rising?
- Is there a high rate of failure?
- Are there ways to reduce failed fusions?
- What is the cost of implants?

Following discussion, Rose Hatmaker and Kimberly Olson offered to work together to bring to the next meeting comparative cost, frequency and outcome data for lumbar fusions and other types of lumbar surgery. Daniel Wolfe offered to obtain a recent study comparing the frequency of surgery in Minnesota with other states. Lohman will also look for studies about fusion surgery outcomes.

#### **Agenda for the April meeting**

The agenda for the next meeting should include:

- a continuing discussion of lumbar spine surgery;
- the revised spinal stimulator and intrathecal drug delivery system rule language;
- a data privacy presentation; and
- information about epidural injections.

#### **Adjournment**

A motion to adjourn the MSRB meeting at 6 p.m. was approved.

Respectfully submitted,  
Kate Berger  
General Counsel  
Department of Labor and Industry

Comments Received and Actions Taken Re: Proposed Rules for Spinal Cord Stimulators

	<b>Comment</b>	<b>Recommendation</b>
<p>p. 1 1.30</p>	<p>Change “and is not a candidate for any other surgical therapy” to “Recommended only for selected patients in cases when less invasive procedures have failed or are contraindicated”. Use of SCS should not be limited to cases in which <u>all</u> other therapies are no longer available.</p>	<p>No action taken.</p>
<p>p. 1 1.31</p>	<p>Who does the psychological evaluation?</p>	<p>Clarify that this is done by the treating health care provider.</p>
<p>p. 1, 1.31</p>	<p>What if the provider doesn't feel capable of making this determination?</p>	<p>Clarify that the provider can obtain a consult if desired.</p>
<p>Added by Department</p>		
<p>p. 1, 1.35-37</p>	<p>What constitutes an appropriate trial period?</p>	<p>A minimum trial period of three days</p>
<p>p. 1, 1.35-37</p>	<p>When is a trial judged to be successful?</p>	<p>At least 50% relief of pain</p>
<p>p. 1, 1.29</p>	<p>Provide a definition of “intractable pain”</p>	<p>Use the definition provided in MS 152.125 “... ‘intractable pain’ means a pain state in which the cause of the pain cannot be removed or otherwise treated with the consent of the patient and in which, in the generally accepted course of medical practice, no relief or cure of the cause of the pain is possible, or none has been found after reasonable efforts.”</p>

MSRB Meeting 4/17/07

Comments Received and Recommendations Re: Proposed Rules for Intrathecal Drug Delivery Systems

	<b>Comment</b>		<b>Recommendation</b>
p. 2, 1. 13	Added by Department What constitutes an appropriate trial period? Which intrathecal medications are allowed?		A minimum trial period of 24 hours Only morphine and hydromorphone for spinal conditions; only morphine, hydromorphone and ziconotide for CRPS. Other medications can be used only with prior approval.

Comments Received and Recommendations Re: Proposed Rules for Spinal Cord Stimulators

	<b>Comment</b>	<b>Actions Taken</b>
p. 1 l. 31	What are the psychological contraindications?	No change. While guidelines state that "evident unresolved major psychiatric comorbidity" is a contraindication, specific disorders are not identified in the guidelines. This is a clinical judgment made on an individualized basis given all of the clinical facts of the case.
p. 1 l. 31	The proposed rule does not require psychological testing but leaves it to the discretion of the provider. The provider may not have had sufficient time with the patient to detect adverse psychological factors.	No action.

Comments Received and Actions Taken Re: Proposed Rules for

	<b>Comment</b>	<b>Recommendation</b>
p. 1 1. 15	Replace “dorsal column stimulator” with “spinal cord stimulation” and “morphine pump” with “intrathecal drug delivery system”. The terms “dorsal column stimulator” and “morphine pump” are obsolete.	Accept.
p. 1 1. 15	Replace “dorsal column stimulator” with “neurostimulation”.	Reject. “Neurostimulation” is a broad term that could be construed to include modalities such as TENS units. This would create confusion in the application of the rules
p. 1 1. 24	Replace references to somatic and neuropathic pain with “intractable” pain. These distinctions are no longer considered clinically significant.	Accept.
p. 1 1. 23-39	Change “and is not a candidate for any other surgical therapy” to “where more conservative treatments have been tried”. Use of SCS should not be limited to cases in which <u>all</u> other therapies are no longer available.	(Deferred to later discussion)
p. 1 1. 23-39	Change “personality or psychosocial” to “psychological”	Accept
p. 2 1. 23-39	Change “is likely to benefit from this treatment” to “has no psychological contraindications to this treatment.”	Accept

MSRB Meeting 10/22/09  
 Comments Received and Actions Taken Re: Proposed Rules for Intrathecal Drug Delivery Systems

<b>Comment</b>	<b>Recommendation</b>
<p>Pump failure is rare, catheter complications are estimated to occur in 20% of cases (Follett KA, et al. J Pain and Symptom Management 2000; 3: 209-215).</p>	<p>No action</p>
<p>Recommend allowing bupivacaine and clonidine to be used at the discretion of the implanting physician. The second line drugs bupivacaine and clonidine are supported by class III evidence and should be allowed depending on implanter preference. Baclofen should be allowed for patients with spasm as a component of their pain problem. Medicare policy allows 6 drugs to be used in pumps: Morphine, Hydromorphone, Fentanyl, Bupivacaine, Clonidine, Baclofen</p>	<p>Recommendation: The rules should be silent on which medications can be used in a pump.</p>
<p>Added by Department</p>	
<p>p. 2, 1. 13.</p>	<p>Recommendation: A minimum trial period of 24 hours.</p>
<p>What constitutes an appropriate trial period?</p> <p>There is no reliable evidence for long-term efficacy</p>	<p>Recommendation: DLI should work with IDDS providers to determine under what circumstances supplemental opiate analgesics via another route of administration can be used by patients with a pump and when a pump should be removed because it has failed to meet the goals of therapy.</p>

REPORT

*Intrathecal Drug delivery Systems*

July 16, 2009

The Department has prepared this report on intrathecal drug delivery systems in accordance with the guidelines and formats used in the MSRB Charge to its Medications Task Force (October 14, 2004 MSRB meeting). The overall clinical question considered in this review was:

1. What is the proper use of intrathecal drug delivery systems in the treatment of chronic spinal pain and complex regional pain syndrome (reflex sympathetic dystrophy)?

This overall question was addressed by identifying and synthesizing the best available medical data on the following specific issues:

Are intrathecal drug delivery systems *effective* in the treatment of chronic spinal pain and complex regional pain syndrome (reflex sympathetic dystrophy)?

Are intrathecal drug delivery systems *safe*?

What is the appropriate trial period for determining if a patient will have a favorable response to treatment with intrathecal drug delivery systems?

What are the appropriate criteria for judging whether a patient had a favorable response during a trial period?

### Department Work Plan

The Department used the same “evidence-based medicine” approach to intrathecal drug delivery systems as had been employed by the MSRB’s Medications Task Force in preparing its report on non-steroidal anti-inflammatory drugs (NSAIDs)<sup>1</sup>. Evidence-Based Medicine (EBM) “is the process of systematically reviewing, appraising and using clinical research findings to aid the delivery of optimum clinical care to patients.”<sup>2</sup> EBM replaces clinical intuition, observations from personal clinical experience, and hypothetical arguments based on pathophysiological principles, as the principle grounds for clinical decision-making. Instead evidence from systematic surveys and critical appraisals of peer-reviewed, methodologically-sound clinical research is gathered, reviewed and synthesized using standardized, objective protocols based on agreed rules of evidence.

Key components of the evidence-based medicine approach used by the Department are:

- a) the systematic search for, and retrieval of, all the relevant medical literature regarding the use of spinal cord stimulators that addresses one or more of the specific issues listed above;
- b) sorting the retrieved literature by level of evidence;
- c) critical appraisal of that literature to systematically examine its validity, results and relevance; and,
- d) synthesis of the findings, with a grade of recommendation.

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1 Final Report. MSRB Task Force On Medications. Nonsteroidal Anti-Inflammatory Drugs, July 21, 2005

2 Rosenberg W, Donald A. “Evidence-based medicine: an approach to clinical problem solving” BMJ 1995; 310(6987): 1122–1126  
Strauss SE, Richardson WS, Glasziou P, Haynes RB Evidence-based Medicine: How to Practice and Teach EBM Edinburgh; Churchill Livingstone, 2005

The search and retrieval of the medical literature was done using computerized search engines and on-line bibliographical databases of the medical literature. In order to maximize the efficient use of time and resources, the same strategies as used by the MSRB's Medications Task Force in its analysis on NSAIDs were adopted to target the searches to the best and most recent evidence by using a step-wise search process.

First, the Department searched the medical literature by "level of evidence." The levels of evidence (Table 1) are a hierarchy representing the strength of the conclusion that can be drawn from a study of that type. Level I evidence is the most compelling, while Level VI evidence is the weakest. The Department restricted the initial search of the medical literature to Level I evidence – systematic reviews and meta-analyses. A systematic review is itself a review of the medical literature conducted using methods (including systematic search and retrieval of all the relevant primary source evidence and critical appraisal of the evidence found using standardized techniques) designed to minimize the likelihood of bias in the results. A meta-analysis is a systematic review in which quantitative methods are used to summarize the results of the review<sup>3</sup>. Not only are systematic reviews and meta-analyses the strongest evidence available but they have the additional property of representing the other levels of evidence.

Table 1: Levels of Evidence<sup>4</sup>

I	systematic reviews/meta-analyses of multiple randomized, controlled trials
II	randomized, controlled trials
IIIA	controlled studies without randomization
IIIB	other types of quasi-experimental study
IV	non-experimental descriptive studies
V	case series
VI	expert committee reports or opinions/clinical experience of respected authorities, or both

Using Level I evidence means that the Department could review efforts by other researchers who had already searched the medical literature for Level II and higher evidence, retrieved and reviewed these studies to determine their relevance and methodological quality, abstracted and evaluated their findings, and synthesized the results. This allowed the Department to leverage its resources to review a much larger body of evidence.

Second, the Department tried to focus the search on the most recent studies, so as to best represent the most current information.

The Department also searched for any already published, evidence-based guidelines for the use of intrathecal drug delivery systems.

<sup>3</sup> Guyatt G, Rennie D *Users' Guides to the Medical Literature. Essentials of Evidence-Based Clinical Practice* AMA Press, 2002  
FOCUS "Critical Appraisal Tool" at <http://www.focusproject.org.uk/>

<sup>4</sup> Adapted from Phillips B, Ball C, Sackett D, Badenoch D, Straus S, Haynes B, Dawes M "Levels of Evidence and Grades of Recommendation" Oxford Centre for Evidence-based Medicine, 1998 [http://www.cebm.net/levels\\_of\\_evidence.asp](http://www.cebm.net/levels_of_evidence.asp)

Prior to beginning the literature search, the Department adopted a set of guidelines for determining when and how the searches would be extended that were similar to those used by the MSRB's Medications Task Force in its analysis on NSAIDs. If at least 10 valid and unrelated references to systematic reviews were not found, the search would be extended to look for all articles in category II (randomized controlled trials) and for all articles in category I (systematic reviews) in the entire database.

The search for relevant medical literature was in fact extended to all levels of evidence. And the search was extended back in time to encompass all of the available literature in the on-line databases.

The Department conducted the literature searches in two electronic bibliographic databases:

1. Medline through the PubMed portal at <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi> ; and,
2. The Cochrane Library (The Cochrane Database of Systematic Reviews, Database of Abstracts of reviews of Effects, and The Cochrane Central Register of Controlled Trials) through the Lumina portal of the University of Minnesota Libraries at [http://tc.liblink.umn.edu/sfx\\_local/a-z/default](http://tc.liblink.umn.edu/sfx_local/a-z/default).

PubMed is a service of the National Library of Medicine (NLM) available via the National Center of Biotechnology's Entrez retrieval system. PubMed is a public access search engine for MEDLINE, NLM's premier bibliographic database for medical literature. MEDLINE contains bibliographic citations and author abstracts from more than 4,800 biomedical journals published in the United States and 70 other countries. The database contains over 12 million citations dating back to mid-1960.

The Cochrane Library consists of a regularly updated collection of evidence-based medicine databases created by the Cochrane Collaboration, an international non-profit independent organization of health care providers and health care researchers. The Cochrane Library is a collection of evidence-based medicine databases, which is up-dated quarterly from the best available information about healthcare interventions found in both published and unpublished medical studies from around the world. The Cochrane Database of Systematic Reviews (CDSR) is the collection of systematic reviews done by Cochrane Collaboration work groups. The Database of Abstracts of Reviews of Effects (DARE) contains summaries of systematic reviews done by others, which have met strict quality criteria established by the Cochrane Collaboration. Included reviews have to be about the effects of interventions. The Cochrane Central Register of Controlled Trials (CENTRAL) includes details of clinical trials found in bibliographic databases (notably MEDLINE and EMBASE), and other published and unpublished sources.

The Department used the same inclusion criteria used by the MSRB's Medications Task Force in its analysis on NSAIDs to determine which of the studies found in the automated searches would be retrieved for further analysis. First, the title of the article was reviewed to confirm that the article was about the therapeutic use of intrathecal drug delivery systems in humans. The abstracts and bibliographical data were then retrieved for articles meeting the first screening and reviewed to determine if:

- the article addressed one of the specific issues of relevance about intrathecal drug delivery systems;
- the article represented a study of the appropriate level of evidence;
- it was a study published during the search time frame;
- the article was published in English; and
- the article was available on-line through the University of Minnesota Bio-Medical Library.

Articles selected for inclusion after a review of the article abstract were retrieved in electronic format from the University of Minnesota Bio-Medical Library through the Lumina portal. An electronic database was created listing the authors, the title of the article, and the journal reference. Each article's abstract and full text was then hyperlinked to its citation in the database. Retrieved articles were evaluated for their level of evidence and assigned a "relevance" category. Systematic reviews (and/or meta-analyses) and randomized controlled trials were considered to be of "high" relevance. Other types of controlled trials and economic evaluations were considered to be of "medium" relevance. Unsystematic reviews, editorials, case series, case studies and all other types of articles were considered to be of "low" relevance.

An additional computerized search for guidelines, using the key words "pain" and "intrathecal drug delivery systems" was conducted in PubMed and at the websites of organizations known to be active in guideline development, appraisal, or cataloging:

<b>Country</b>	<b>Name of organization</b>	<b>Website</b>
Netherlands	Dutch Institute for Healthcare Improvement	<a href="http://www.cbo.nl">http://www.cbo.nl</a>
New Zealand	New Zealand Guidelines Group	<a href="http://www.nzgg.org.nz">http://www.nzgg.org.nz</a>
	Accident Compensation Corporation	<a href="http://www.acc.co.nz/index.htm">http://www.acc.co.nz/index.htm</a>
Scotland	Scottish Intercollegiate Network	<a href="http://www.sign.ac.uk">http://www.sign.ac.uk</a>
Sweden	Swedish Council on Technology Assessment in Health Care	<a href="http://www.sbu.se">http://www.sbu.se</a>
UK	National Library of Guidelines	<a href="http://www.library.nhs.uk/guidelinesfinder">http://www.library.nhs.uk/guidelinesfinder</a>
USA	National Institutes of Health Consensus Development Program	<a href="http://consensus.nih.gov">http://consensus.nih.gov</a>
	National Guideline Clearinghouse	<a href="http://www.guideline.gov">http://www.guideline.gov</a>
	Agency for Healthcare research & Quality	<a href="http://www.ahrq.gov/">http://www.ahrq.gov/</a>

Finally, the computerized searches were supplemented by hand searches of the bibliographies of key articles (particularly systematic reviews and guidelines) and with any articles submitted by interested parties.

Articles chosen for analysis were then assessed for their quality using criteria that were appropriate to the study type.

For systematic reviews, the quality criteria chosen were:

<b>1. Study Identification</b>	
Multiple electronic databases	
Unbiased explicit searching strategies	
Hand searches	
Attempts to include "gray" literature	
Estimation of potential publication bias	
<b>2. Study selection</b>	
Only randomized controlled trials included	
Explicit inclusion/exclusion criteria	
Selection criteria applied uniformly	
Rationale for excluding studies	
<b>3. Appraisal of studies</b>	
Described in detail	
Uniformly applied to all studies	
Important parameters addressed	
<ul style="list-style-type: none"> <li>• random allocation</li> <li>• double blinding</li> <li>• relevant outcome measures</li> <li>• follow-up of at least 80 per cent of participants</li> <li>• analysis consistent with the study design</li> </ul>	_____ _____ _____ _____ _____
Effect of study quality on conclusions assessed	
<b>4. Data Collection</b>	
Was missing information considered?	
<b>5. Data synthesis</b>	
Assessment for heterogeneity	
All valid studies used	
Sensitivity analysis performed	
Variations between studies considered	

For randomized controlled trials, the quality criteria were:

Random allocation	
Minimal dropouts (< 15%)	
Blinding of patient	
Blinding of the assessor	
Co-treatments have been used in an equivalent manner among treatment groups.	
Assessment of the extent of patient adherence to the prescribed therapy	
No unintended crossovers from one study treatment to the other.	
Adequate consideration of statistical and clinical significance of findings.	
Adequate demographic description of patients, including at least age, gender, and referral source.	
Adequate clinical description, including pain duration, neurologic deficits, sciatica, previous surgery, and other inclusion or exclusion criteria.	
Adequate description of treatment in terms of dosage, duration, frequency, and technique.	
Reporting of all relevant outcomes, which may include symptoms, physiologic changes, functional ability, costs of care, and psychological measures.	

These criteria were adapted from recommendations for critical appraisal of systematic reviews and randomized controlled trials found in the peer-reviewed literature and textbooks of evidence-based medicine.<sup>5</sup>

For guidelines, the quality criteria were derived from the instrument developed by The AGREE Collaboration started in 1998 as a research project under the Biomedicine and Health Research (BIOMED 2) Programme, funded by the European Union<sup>6</sup>:

<b>Scope and purpose</b>	
Objective(s) of the guideline are specifically described.	
The clinical question(s) is specifically described.	
The patients to whom the guideline is meant to apply is specifically described.	
<b>Stakeholder involvement</b>	
The guideline development group includes individuals from all the relevant professional groups.	
The patients' views and preferences are sought.	
<b>Rigour of development</b>	
Systematic methods are used to search for evidence.	
The criteria for selecting the evidence are clearly described.	
The methods used for formulating the recommendations are clearly described.	
The health benefits, side effects and risks are considered in formulating the recommendations.	
There is an explicit link between the recommendations and the supporting evidence.	
The guideline was externally reviewed by experts prior to publication.	
A procedure for updating the guideline is provided.	
<b>Clarity and presentation</b>	
The recommendations are specific and unambiguous.	
The different options for diagnosis and/or treatment of the condition are clearly presented.	
Key recommendations are easily identifiable.	
<b>Applicability</b>	
The target users of the guideline are clearly defined.	
The potential organizational barriers in applying the recommendations are discussed.	
The potential cost implications of applying the recommendations were considered.	
The guideline is supported with tools for application.	
The guideline presents key review criteria for monitoring and audit purposes	
The guideline was piloted among end users.	
<b>Editorial independence</b>	
The guideline is editorially independent from the funding body.	
Conflicts of interest of guideline development members are recorded.	

Articles were scored "yes", "no", "can't tell" on each item. A summary score was determined by adding together the "yes" responses, dividing by the total number of criteria. This scoring system is a short hand way of indicating overall study quality and is similar to systems used in many systematic reviews for evaluating primary source literature.

<sup>5</sup> Oxman AD, Cook DJ, Guyatt GH "Users' guides to the medical literature. VI How to use an overview" *Journal of the American Medical Association* 1994; 272(17): 1367-1371

Guyatt GH, Sackett DL, Cook DJ "Users' guides to the medical literature. II. How to use an article about therapy or prevention. A. Are the results of the study valid?" *Journal of the American Medical Association* 1993; 270(21): 2598-601.

Crombie IK *The Pocket Guide to Critical Appraisal: A Handbook for Healthcare Professionals* London; BMJ Publishing Group, 1996

<sup>6</sup> <http://www.agreecollaboration.org/>

In addition, the author's conclusions regarding intrathecal drug delivery systems were abstracted, and, in the case of the systematic reviews, the primary literature relied upon by the author(s) in reaching their conclusions was identified and tabulated. The results of the quality review, the author's conclusions, and, if relevant, the bibliography of the primary source literature were entered into a "Summary Sheet" for each article. These Summary Sheets were then also hyperlinked to the Department database.

Finally, the abstracted conclusions from each article were transferred to a separate spreadsheet. There, the conclusions were arranged thematically into columns for comparison across articles.

## Results

The first PubMed search used a search string published in the medical literature that has been validated as both sensitive and specific for retrieving systematic reviews.<sup>7</sup> The search string was combined first with the key words "intrathecal drug delivery" and "pain" while limiting the results to systematic reviews since 1990. Because this search yielded less than 10 unique references, the search for systematic reviews was expanded to the entire Pub Med database. This still yielded less than 10 unique references so the search was expanded to include RCTs since 1990. Finally, since this search yielded only 10 unique references, the search was expanded to include all articles on "intrathecal drug delivery" and "pain" since 1990. The same process was repeated using the search terms "intrathecal medication" and "pain". The results of the searches can be found in the documents "IDD and pain - reviews.doc", "IDD and pain – RCTs.doc", "IDD and pain.doc" "IM and pain - reviews.doc", "IM and pain – RCTs.doc", and "IM and pain.doc". (see Appendix 1).

These searches retrieved 714 titles, some found more than once. Of these, 83 articles were presumed relevant based on their title and retrieved for further review.

The searches of the Cochrane Database of Systematic Reviews (CDSR) of the Database of Abstracts of Reviews of Effects (DARE) were done using the key word "intrathecal drug delivery" and did not yield any references not found in the PubMed search.

The search for guidelines in PubMed and on the World Wide Web found 13 references of which 5 were earlier versions of guidelines whose later versions were included in the analysis.

References for all the articles chosen for further review were combined in an Excel database, intrathecal drug delivery.xls (see Appendix 2). Of the 96 articles (6 systematic reviews, 6 randomized controlled trials, 13 guidelines, 2 clinical trials, 1 registry study, 2 economic

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<sup>7</sup> " ((meta-analysis [pt] OR meta-analysis [tw] OR metanalysis [tw]) OR ((review [pt] OR guideline [pt] OR consensus [ti] OR guideline\* [ti] OR literature [ti] OR overview [ti] OR review [ti]) AND ((Cochrane [tw] OR Medline [tw] OR CINAHL [tw] OR (National [tw] AND Library [tw])) OR (handsearch\* [tw] OR search\* [tw] OR searching [tw]) AND (hand [tw] OR manual [tw] OR electronic [tw] OR bibliographi\* [tw] OR database\* OR (Cochrane [tw] OR Medline [tw] OR CINAHL [tw] OR (National [tw] AND Library [tw]))))) OR ((synthesis [ti] OR overview [ti] OR review [ti] OR survey [ti]) AND (systematic [ti] OR critical [ti] OR methodologic [ti] OR quantitative [ti] OR qualitative [ti] OR literature [ti] OR evidence [ti] OR evidence-based [ti]))) BUTNOT (case\* [ti] OR report [ti] OR editorial [pt] OR comment [pt] OR letter [pt]) " found in Shojania KG, Bero LA. "Taking advantage of the explosion of systematic reviews: an efficient MEDLINE search strategy" *Eff Clin Pract* 2001;4(4): 157-62.

evaluations, 36 unsystematic reviews/editorials, and 30 case series/studies), the full article was available electronically for 70 of them through the Lumina portal at the University of Minnesota (5 systematic reviews, 6 randomized controlled trials, 13 guidelines, 1 registry study, 2 economic evaluations, 16 unsystematic reviews/editorials, and 27 case series/studies). When available, the full article was hyperlinked to the database. The article's abstract was then reviewed to determine level of evidence and the relevance of the article.

In all, 21 articles met all of the inclusion criteria and were not versions of other references (5 systematic reviews, 5 randomized controlled trials, 8 guidelines, 1 registry study, and 2 economic evaluations) and were entered into a second Excel database, intrathecal drug delivery - review.xls (see Appendix 3). When more than one version of a study was available, the most complete and most recent version was used. In addition, two references available only as abstracts were included as they represented high quality studies (1 systematic review and 1 clinical trial). A quality review was then performed for each article. One clinical trial available as an abstract only was omitted as it was an earlier version of the one included.

The retrieved articles varied in quality. The RCTs had relatively high summary quality scores ranging from 10/12 to 12/12. Four of the systematic reviews had poor summary quality scores ranging from 1/22 to 5/22; the fifth had a moderate score of 11/23. The guidelines had the most variation in summary quality scores, ranging from 9/23 to 20/23; 2 had high scores, while four had scores of 11/23 or less.

The systematic reviews and guidelines referenced a combined total of 426 primary studies. These are listed on the summary sheet for individual systematic reviews and guidelines and for all of the systematic reviews and guidelines in an Excel database intrathecal drug delivery – primary sources.xls (see Appendix 5) with a listing for each primary study of the systematic reviews and guidelines in which it is referenced as data.

Quality review was not done for the registry study, the two economic evaluations, or the two studies only available as abstracts.

Overall, all of the systematic reviews and 4 of the RCTs addressed the question of effectiveness. Two of the systematic reviews and four of the RCTs addressed issues of safety. Only one of the systematic reviews reported on the appropriate trial period and the criteria used for judging whether a patient had a favorable response during a trial period.

The evidence used in developing the recommendations in the guidelines analyzed was referenced in the available text for 7 of the 8 guidelines. Those guidelines relied, at least in part, on systematic reviews and RCTs. Four of the 7 with references used at least one systematic review; 6 of 7 used at least one RCT; and 4 of 7 referenced other guidelines or previous versions of the guideline being analyzed. In some cases those systematic reviews, RCTs, and guidelines were the same ones identified in the searches done for this report (as noted in columns J, K, and M of intrathecal drug delivery - review.xls).

The findings made by the article's author(s) were then abstracted and entered into a third database, intrathecal drug delivery - analysis.xls (see Appendix 4). There, the findings were

arranged thematically into columns for comparison across articles. Themes were identified inductively from the abstracted conclusions by arranging them into the fewest mutually exclusive categories.

The themes identified were:

<i>theme</i>	<i># articles</i>	<i>summary quality scores</i>
Quantitative results	SysRev: 3 RCT: 5 Guidelines: 1	SysRev: 5/22 – 11/22 RCT: 10/12 – 12/12 Guidelines: 11/23
Reported complications	SysRev: 2 RCT: 4 Guidelines: 4	SysRev: 1/22 – 9/22 RCT: 10/12 – 12/12 Guidelines: 9/23-18/23
Study design issues	SysRev: 3 RCT: 5 Guidelines: 4	SysRev: 2/22 – 10/22 RCT: 10/12 – 12/12 Guidelines: 11/23-20/23
Author's overall conclusions	SysRev: 4 RCT: 5 Guidelines: 8	SysRev: 1/22 – 11/22 RCT: 10/12 – 12/12 Guidelines: 9/23 – 20/23
Comments on length of trial period	SysRev: 1 RCT: 0 Guidelines: 4	SysRev: 11/22 Guidelines: 9/23 – 11/23
Comments on judging trial success	SysRev: 1 RCT: 0 Guidelines: 2	SysRev: 11/22 Guidelines: 9/23 – 10/23

### Conclusions

The Department found considerable agreement of published opinion on each issue. While the individual articles varied widely in quality, this variation does not significantly affect the conclusions reached by the authors. Articles of higher quality most often reached the same conclusions as those of lower quality.

The conclusions drawn by the Department from the reviewed literature are:

1. There is limited evidence that permanently implanted intrathecal drug delivery systems are effective in the short-term in achieving at least a 50% reduction in pain in some patients with chronic pain conditions who have a positive response during a screening trial period.

Clin J Pain 2007 Feb 23(2) 180-95    SysRev    The studies reviewed found improvement in pain and functioning on average among patients with chronic noncancer pain who received permanent IDDS.

J Pain Symptom Manage 2000 Aug 20(2) S12-36    SysRev    Intrathecal morphine appears to be safe at clinical concentrations, and has favorable efficacy data. Limited information on the other opioid classes also appears favorable, although published literature supporting this is very limited. Based on the currently available literature, both clinical efficacy and toxicology for bupivacaine and clonidine appear favorable. The efficacy of combinations of different drug classes such as opioids/local anesthetics, opioids/clonidine, and opioids/local anesthetics/ clonidine appears favorable, but is based largely on case studies and retrospective analysis.

<u>Health Technology Assessment 2000: Vol. 4: No. 32</u>	SysRev	Such data as are available indicate a generally positive effect of the therapy, with side effects and complications occurring in about a quarter of the recipients, but it is difficult to draw definite conclusions because the quality of the data is so poor.
<u>Anesth Analg 2000 Dec 91(6) 1493-8</u>	RCT	The combination of morphine and clonidine produced significantly more pain relief than placebo 4 h after administration; either morphine or clonidine alone did not produce as much pain relief.
<u>J Clin Oncol 2002 Oct 1 20(19) 4040-9</u>	RCT	IDDSs improved clinical success in pain control, reduced pain, and significantly relieved common drug toxicities in patients with refractory cancer pain.
<u>J Pain Symptom Manage 2006 May 31(5) 393-406</u>	RCT	Slow titration of ziconotide, a nonopioid analgesic, to a low maximum dose resulted in significant improvement in pain and was better tolerated than in two previous controlled trials that used a faster titration to a higher mean dose.
<u>JAMA 2004; 291:63-70</u>	RCT	Intrathecal ziconotide provided clinically and statistically significant analgesia in patients with pain from cancer or AIDS.
<u>Pain Physician. 2007 Jan;10(1):7-111</u>	Guide	The evidence for implantable intrathecal infusion systems is strong for short-term improvement in pain of malignancy or neuropathic pain.
<u>Guidelines For Longterm Intrathecal Infusions (PM6)</u>	Guide	A range of non-opioid spinal analgesic agents are utilized for long-term therapy, some of which are supported by low levels of evidence and for which safety has not been fully established. There is level II evidence for efficacy in treating neuropathic pain with intrathecal clonidine; neuropathic pain following spinal cord injury with morphine and clonidine combined; neuropathic pain with ziconotide. Intrathecal administration of opioids and local anaesthetics and / or clonidine could be considered as an alternative agent in patients with poorly controlled neuropathic pain ... following spinal cord injury. Many of these combinations are ... "off label" ...
<u>Assessment and management of chronic pain.</u>	Guide	Intrathecal Medication Delivery Systems can provide an excellent therapeutic effect for nonmalignant and cancer pain. However, it should be reserved only for patients who have failed other conservative approaches for the treatment of pain, and should be used cautiously. The best candidates are patients who respond well to oral opioids but who cannot tolerate the side effects (e.g., sedation, nausea, constipation).
<u>Complex Regional Pain Syndrome type 1 Guidelines</u>	Guide	Intrathecal baclofen has no place in the treatment of patients with CRPS-I. Intrathecal baclofen can only be considered for patients with CRPS-I if dystonia is a major problem and conventional therapy has proven ineffective. This treatment must be administered in the context of a trial.
<u>Treatment in Workers' Compensation 2006</u>	Guide	Recommended only as an end-stage treatment alternative for selected patients. This treatment should only be used relatively late in the treatment continuum, when there is little hope for effective management of chronic intractable pain from other therapies. The specific criteria in these cases include the failure of at least 6 months of other conservative treatment modalities, intractable pain secondary to a disease state with objective documentation of pathology, further surgical intervention is not indicated, psychological evaluation unequivocally states that the pain is not psychological in origin, and a temporary trial has been successful prior to permanent implantation as defined by a 50-70% reduction in pain.
<u>Evidence-based clinical practice guideline for interdisciplinary rehabilitation of chronic non-malignant pain syndrome patients</u>	Guide	Given the continued absence of quality research, however, the current guidelines do not recommend using implantable infusion pumps or spinal cord stimulators with chronic non-malignant pain syndrome patients.
<u>Intrathecal drug delivery for the management of pain and spasticity in adults: recommendations for best clinical practice</u>	Guide	Intrathecal drug delivery can be an effective method of pain control. Patient selection is important, particularly when used for CNMP. It must be carried out by a multi-professional team with a comprehensive understanding of the physical, psychological and rehabilitation aspects of the patient's condition.
<u>Pain Med 2004 5 6-13.</u>	Registry	Current clinical practices related to trialing of drug-delivery systems resulted in the majority of patients successfully trialed. At 12-month follow-ups, implanted patients experienced reductions in numeric back and leg pain ratings, improved Oswestry scores, and high satisfaction with the therapy.

2. There is no reliable evidence that permanently implanted intrathecal drug delivery systems are effective in the long-term in achieving at least a 50% reduction in pain in patients with chronic pain conditions who have a positive response during a screening trial period.

<u>Clin J Pain</u> 2007 Feb 23(2) 180-95	SysRev	Methodologic limitations preclude conclusions concerning the effectiveness of this technology long-term and as compared with other treatments.
<u>J Pain Symptom Manage</u> 2000 Aug 20(2) S12-36	SysRev	No information is available on the long-term compatibility of these combinations.
<u>Pain Physician</u> . 2007 Jan;10(1):7-111	Guide	The evidence is moderate for long-term management of chronic pain.

3. Economic models indicate that permanently implanted intrathecal drug delivery systems are cost-effective in treating patients who have had at least a 50% reduction in pain during a screening trial period.

<u>CLIN THER</u> 1997 19(1) 96-112	CE	When both costs and adverse event rates were set at base case values, the expected cost (discounted at 5%) of IMT over 60 months was \$82,893 (\$1382 per month). With costs and adverse event rates at the best case values, the expected 60-month total cost was \$53,468 (\$891 per month), and when all the values were set at the worst case, the projected total cost rose to \$125,102 (\$2085 per month). By comparison, the cumulative 60-month total cost for medical management was \$85,186.
<u>Neuromodulation</u> 1999; 2:77-84	CE	Decision Analysis: "For the base case and the best case, the cumulative cost with an implanted, programmable pump is less than the cost of medical management after 22 months and 11 months, respectively."  Cost Analysis: "...intrathecal drug delivery becomes more cost effective than oral therapy after 4-6 months have elapsed."

4. There is no reliable evidence that permanently implanted intrathecal drug delivery systems are more effective than alternative treatment options.

<u>J Clin Oncol</u> 2002 Oct 1 20(19) 4040-9	RCT	Sixty of 71 IDDS patients (84.5%) achieved clinical success compared with 51 of 72 CMM patients (70.8%, P = .05). IDDS patients more often achieved >20% reduction in both pain VAS and toxicity (57.7% [41 of 71] v 37.5% [27 of 72], P = .02). The mean CMM VAS score fell from 7.81 to 4.76 (39% reduction); for the IDDS group, the scores fell from 7.57 to 3.67 (52% reduction, P = .055). The mean CMM toxicity scores fell from 6.36 to 5.27 (17% reduction); for the IDDS group, the toxicity scores fell from 7.22 to 3.59 (50% reduction, P = .004). The IDDS group had significant reductions in fatigue and depressed level of consciousness (P < .05).
<u>Guidelines For Longterm Intrathecal Infusions (PM6)</u>	Guide	A range of non-opioid spinal analgesic agents are utilized for long-term therapy, some of which are supported by low levels of evidence and for which safety has not been fully established. There is level II evidence for efficacy in treating neuropathic pain with intrathecal clonidine; neuropathic pain following spinal cord injury with morphine and clonidine combined; neuropathic pain with ziconotide. Intrathecal administration of opioids and local anaesthetics and / or clonidine could be considered as an alternative agent in patients with poorly controlled neuropathic pain ... following spinal cord injury. Many of these combinations are ... "off label"
<u>Assessment and management of chronic pain.</u>	Guide	Intrathecal Medication Delivery Systems can provide an excellent therapeutic effect for nonmalignant and cancer pain. However, it should be reserved only for patients who have failed other conservative approaches for the treatment of pain, and should be used cautiously. The best candidates are patients who respond well to oral opioids but who cannot tolerate the side effects (e.g., sedation, nausea, constipation).

<u>Treatment in Workers' Compensation 2006</u>	Guide	Recommended only as an end-stage treatment alternative for selected patients. This treatment should only be used relatively late in the treatment continuum, when there is little hope for effective management of chronic intractable pain from other therapies. The specific criteria in these cases include the failure of at least 6 months of other conservative treatment modalities, intractable pain secondary to a disease state with objective documentation of pathology, further surgical intervention is not indicated, psychological evaluation unequivocally states that the pain is not psychological in origin, and a temporary trial has been successful prior to permanent implantation as defined by a 50-70% reduction in pain.
<u>Evidence-based clinical practice guideline for interdisciplinary rehabilitation of chronic non-malignant pain syndrome patients</u>	Guide	Given the continued absence of quality research, however, the current guidelines do not recommend using implantable infusion pumps or spinal cord stimulators with chronic non-malignant pain syndrome patients.
<u>Intrathecal drug delivery for the management of pain and spasticity in adults: recommendations for best clinical practice</u>	Guide	Intrathecal drug delivery can be an effective method of pain control. Patient selection is important, particularly when used for CNMP. It must be carried out by a multi-professional team with a comprehensive understanding of the physical, psychological and rehabilitation aspects of the patient's condition.

5. Complications occur in 1/3 or more of cases. Most are side effects of the medication delivered by the system, are dose-dependent, and sometimes improve with continued administration. Catheter, procedure and device related complications are relatively uncommon.

<u>Clin J Pain 2007 Feb 23(2) 180-95</u>	SysRev	The most commonly reported permanent IDDS drug side effects were nausea/vomiting (mean rate weighted by sample size=33%), urinary retention (24%), and pruritus (26%). Catheter problems were also reported commonly. Rare but serious complications included intrathecal catheter tip granulomas.
<u>Pain Physician 2007 Mar 10(2) 357-66</u>	SysRev	Most side effects of intrathecal morphine therapy are dose dependent and mediated by opioid receptors. Common ones include nausea, vomiting, pruritus, urinary retention, constipation, sexual dysfunction, and edema. Less common ones include respiratory depression, and hyperalgesia. Catheter tip inflammatory mass formation is a less common complication that may not be mediated by opioid receptors. Treatment usually involves the utilization of opioid receptor antagonist, such as naloxone.
<u>Eur J Anaesthesiol 2006 Jul 23(7) 605-10</u>	RCT	The incidence of nausea and vomiting was higher at 2- and 4-h observation times, and decreased 24 h after intrathecal injection. No urinary retention was observed in the control group, while 2 h after intrathecal injection urinary retention was observed in 20–40% of cases, and decreased to less than 10% 24 h after spinal injection without differences among the four doses.
<u>Anesth Analg 2000 Dec 91(6) 1493-8</u>	RCT	The most common side effects after morphine administration in those with SCI were pruritus, oxygen desaturation, sedation, nausea, and hypotension (>15% decrease in blood pressure). The most common side effects after clonidine administration were hypotension, nausea, sedation, oxygen desaturation, and dry mouth. Of those who received saline, 13% experienced sedation and 13% had oxygen desaturation. The most common side effects after the administration of the mixture were hypotension, oxygen desaturation, pruritus, dry mouth, and sedation. Using the mixture did not result in a marked reduction in the incidence of side effects.
<u>J Pain Symptom Manage 2006 May 31(5) 393-406</u>	RCT	Significant adverse events reported in the ziconotide group were dizziness, confusion, ataxia, abnormal gait, and memory impairment. Discontinuation rates for AEs and serious AEs were comparable for both groups.
<u>JAMA 2004; 291:63-70</u>	RCT	Nine types of adverse events (fever, hypotension, nausea, vomiting, confusion, dizziness, somnolence, abnormal gait, and urinary retention) occurred with significantly greater frequency in the ziconotide group compared with the placebo group, but starting at the lower dosage, using smaller dose increments, and increasing the interval between dose titrations tended to reduce this frequency.

<a href="#">Pain Physician. 2007 Jan;10(1):7-111</a>	Guide	The complications include post-dural puncture headache, infection, nausea, urinary retention, pruritus, catheter and pump failure, pedal edema, hormonal changes, granuloma formation, and decreased libido.
<a href="#">Guidelines For Longterm Intrathecal Infusions (PM6)</a>	Guide	Intrathecal drug administration can result in significant undesirable side effects, and has the possibility of morbidity and mortality.
<a href="#">Complex Regional Pain Syndrome type 1 Guidelines</a>	Guide	The main side-effects of the screening process and continuous administration of ITB are post-puncture headache, diminished consciousness and urine retention.
<a href="#">Intrathecal drug delivery for the management of pain and spasticity in adults: recommendations for best clinical practice</a>	Guide	Minor complications are common. In a population of cancer patients, catheter, procedure, device-related and illness-associated adverse incidents occurred at a rate of 0.45 events per patient year. Neurological deficits can occur from the procedure and from inflammatory mass development at catheter tip. There are reports of neurotoxicity and permanent neurologic al damage following intrathecal infusions of local anaesthetics. Possible infections include meningitis, epidural abscess, pump pocket infection or pump reservoir infection. Cerebrospinal fluid leaks, hygromas and post dural puncture headaches have all been reported. Device-related complications include catheter kinking, disconnection, dislodgement or pump failure, program error and overfill or incorrect refill.
<a href="#">Pain Med 2004 5 6-13.</a>	Registry	Adverse events were reported in 23 patients receiving an IDDS implant. Of these, 21 required some surgery to correct the problem. Adverse events included: Infection (2.2%), dislodgment/ migration (1.5%), and cerebrospinal fluid leak (0.7%). The most common adverse event over 12 months was reaction to medication, which occurred in 5.1% of patients. Other, rarely reported events included catheter kinking in 1.5% and catheter fracture in 0.7% of patients.

6. Trial screening periods in the reported case series and clinical trials have lasted from a single injection up to 10 days, with most being 24 hours or less. There is no information to judge whether the length of the trial period influences the reported efficacy of implanted intrathecal drug delivery systems.

<a href="#">Health Technology Assessment 2000: Vol. 4: No. 32</a>	SysRev	In those studies reporting a trial, 23 used a single injection and 7 an infusion for more than 24 hours - of those 6 lasted for more than 48 hours
<a href="#">Guidelines For Longterm Intrathecal Infusions (PM6)</a>	Guide	Prior to the insertion of long term delivery systems ... Intrathecal trials should be undertaken to assess appropriate drugs, doses and efficacy of the drug or drug combinations. Testing with temporary catheter systems allows investigation of the potential side effects of the proposed procedure and medication.
<a href="#">Treatment in Workers' Compensation 2006</a>	Guide	The specific criteria include ... a temporary trial has been successful prior to permanent implantation.
<a href="#">Intrathecal drug delivery for the management of pain and spasticity in adults: recommendations for best clinical practice</a>	Guide	A trial of intrathecal therapy should always be performed. This can be by means of bolus or infusion but the former give limited information. There is no ideal screening method.
<a href="#">Neuromodulation 2007 10(4) 300-328</a>	Guide	The panelists felt that trial procedure should be left up to the physician performing them. The panelists felt that until there are data that suggest that trials are unnecessary, trials should be performed before placing IT delivery agents through an IDDS. Trials can be performed with monotherapy or with polyanalgesia.
<a href="#">Pain Med 2004 5 6-13.</a>	Registry	Trialing methodologies were: Continuous epidural infusion (53%), continuous intrathecal infusion (25%), single intrathecal bolus injection (14%), and multiple intrathecal bolus injections (8%). The majority of patients (81.1%) were trialed with morphine only. The mean duration of the trial was 3.5 ± 5.4 days.

7. The most common measure of success in the trial period was relief of pain and the most common criteria was pain relief of at least 50%.

<u>Health Technology Assessment 2000: Vol. 4: No. 32</u>	SysRev	Those studies reporting a criteria for judging success used 50% relief of pain.
<u>Guidelines For Longterm Intrathecal Infusions (PM6)</u>	Guide	Base line levels of pain, function and Quality of Life should be recorded.
<u>Treatment in Workers' Compensation 2006</u>	Guide	Defined by a 50-70% reduction in pain

8. There is limited evidence to support the use of morphine, hydromorphone and ziconotide as first line agents in intrathecal drug delivery systems.

- (a) There is no evidence to support the use of other medications as first line agents.
- (b) There is no reliable evidence on which medications are indicated when morphine, hydromorphone and ziconotide are not effective or become ineffective.

<u>reference</u>	<u>type</u>	<u>author's conclusions</u>
<u>Guidelines For Longterm Intrathecal Infusions (PM6)</u>	Guide	There is level II evidence for efficacy in treating neuropathic pain with intrathecal clonidine; neuropathic pain following spinal cord injury with morphine and clonidine combined; neuropathic pain with ziconotide.
<u>Complex Regional Pain Syndrome type 1 Guidelines</u>	Guide	Intrathecal baclofen has no place in the treatment of patients with CRPS-I.
<u>Neuromodulation 2007 10(4) 300-328</u>	Guide	The first-line agents are morphine, hydromorphone, and ziconotide. Second line agents include 1) the combination of morphine or hydromorphone and bupivacaine or clonidine; 2) the combination of morphine or hydromorphone and ziconotide; or 3) fentanyl alone. Third-line approaches are: 1) clonidine alone; 2) a combination of morphine/ hydromorphone/ fentanyl/ bupivacaine plus clonidine and ziconotide.
<u>J Pain Symptom Manage 2000 Aug 20(2) S12-36</u>	SysRev	Intrathecal morphine appears to be safe at clinical concentrations, and has favorable efficacy data. Limited information on the other opioid classes also appears favorable, although published literature supporting this is very limited. Based on the currently available literature, both clinical efficacy and toxicology for bupivacaine and clonidine appear favorable. The efficacy of combinations of different drug classes such as opioids/local anesthetics, opioids/ clonidine, and opioids/local anesthetics/ clonidine appears favorable, but is based largely on case studies and retrospective analysis. No information is available on the long-term compatibility of these combinations.
<u>Anesth Analg 2000 Dec 91(6) 1493-8</u>	RCT	Intrathecal morphine resulted in a mean reduction in pain to 80% of the baseline pain before drug administration. Intrathecal administration of clonidine resulted in a mean reduction in pain levels to 83% of the baseline pain. These reductions in pain levels were not significantly different from the relief obtained after saline administration. Intrathecal administration of the mixture of morphine and clonidine resulted in a mean reduction in pain levels to 63% of the baseline pain. There was a significant difference in the relief obtained with the mixture of morphine and clonidine compared with placebo ( $P = 0.0084$ ).

JAMA 2004; 291:63-70

RCT

Mean VASPI scores improved 53.1% (95% CI, 44.0%-62.2%) in the ziconotide group and 18.1% (95% CI, 4.8%-31.4%) in the placebo group (P .001), with no loss of efficacy of ziconotide in the maintenance phase. Pain relief was moderate to complete in 52.9% of patients in the ziconotide group compared with 17.5% in the placebo group (P .001). Five patients receiving ziconotide achieved complete pain relief, and 50.0% of patients receiving ziconotide responded to therapy compared with 17.5% of those receiving placebo (P=.001).

Ann Pharmacother 2006 Jul-Aug 40(7-8) 1293-300

SysRev

In double-blind, placebo-controlled studies, ziconotide significantly improved patient perception of pain from baseline to the end of the study periods, which ranged from 11 to 21 days.

## Recommendations

Based on the conclusions derived from the literature the Department proposes the following draft recommendations to the Medical Services Review Board, to be used as the basis for changes to the Permanent Treatment Parameters governing the use of intrathecal drug delivery systems in workers' compensation claims.

**I. Intrathecal drug delivery systems can effectively relieve pain in selected patients with chronic pain when other options have failed -- at least in the short term.**

**II. An adequate trial period of 24 hours is needed to determine who might benefit from an intrathecal drug delivery system.**

**III. Adequate pain relief of at least 50% during the trial period is needed to determine if a patient might benefit from an intrathecal drug delivery system.**

**V. Morphine, hydromorphone and ziconotide are indicated as first line agents if found to successfully relieve pain by 50% in a trial of at least 24 hours duration.**

**a. There is no indication for other medications as first line agents.**

## **Appendix 1**

The Word files “IDD and pain - reviews.doc”, “IDD and pain – RCTs.doc”, “IDD and pain.doc” “IM and pain - reviews.doc”, “IM and pain – RCTs.doc”, and “IM and pain.doc” list all of the articles found in the literature searches.

## Appendix 2

The Excel workbook intrathecal drug delivery.xls lists all of the articles that were selected by the Department for further review.

**Column A** is an ID number

**Column B** lists the authors of the article.

**Column C** is the title of the article.

**Column D** gives the abbreviated citation as found in Medline and is an active link.

Clicking on the journal citation will call up the abstract and/or article

**Column E** identifies the type of article:

“SysRev” is a systematic review,

“RCT” is a randomized controlled trial

“CCT” is a nonrandomized trial

“Registry” is a registry study

“CE” is an economic evaluation

“SysGuide” is an evidence-based treatment guideline

“Review” is an unsystematic review

“Editorial” is a statement of a single physician’s opinion

“CaseSer” is a case series

“CaseRep” is a single case report

**Column F** indicates whether the article was determined to be relevant for the purposes of this study based on the levels of evidence hierarchy.

**Column G** indicates the availability of the article.

**Column H** is marked with an “X” if the article discusses efficacy.

**Column I** is marked with an “X” if the article discusses safety.

**Column H** includes any comments on the article (especially whether it is an alternate version of another article).

### **Appendix 3**

The Excel workbook intrathecal drug delivery - review.xls lists the results of the quality review of the articles that were selected by the Department for this analysis.

**Column A** is an ID number

**Column B** lists the authors of the article.

**Column C** gives the abbreviated citation as found in Medline and is an active link.

Clicking on the journal citation will call up the abstract and/or article

**Column D** identifies the type of article:

“SysRev” is a systematic review,

“RCT” is a randomized controlled trial,

“SysGuide” is an evidence-based treatment guideline,

“CCT” is a nonrandomized trial,

“Registry” is a registry study,

“CE” is an economic evaluation.

**Column E** is marked with an “X” if the article discusses efficacy.

**Column F** is marked with an “X” if the article discusses safety.

**Column G** is a hyperlink to the summary sheet for the article.

**Column H** is a hyperlink to the summary sheet for the article

**Column I** includes any comments about the article

***For guidelines only:***

**Column J** lists the ID# for any systematic reviews included in this analysis that were used by the authors of the guideline.

**Column K** lists the ID# for any randomized clinical trials included in this analysis that were used by the authors of the guideline.

**Column L** lists the ID# for any economic evaluations included in this analysis that were used by the authors of the guideline.

**Column M** lists the ID# for any guidelines included in this analysis that were used by the author's of the guideline.

## Appendix 4

The Excel workbook [intrathecal drug delivery -analysis.xls](#) lists the author's findings and conclusions regarding the efficacy and safety of spinal cord stimulators, and any other information relevant to the questions posed for this analysis. Wherever possible, the conclusions are stated in the authors' own words.

**Column A** gives the abbreviated citation as found in Medline and is an active link. Clicking on the journal citation will call up the abstract and/or article

**Column B** identifies the type of article:

“SysRev” is a systematic review,

“RCT” is a randomized controlled trial,

“SysGuide” is an evidence-based treatment guideline,

“CCT” is a nonrandomized trial,

“Registry” is a registry study,

“CE” is an economic evaluation.

**Column C** lists the sources of information used.

**Column D** lists any comments made by the authors regarding the sources of information.

**Column E** lists the quantitative results of the study.

**Column F** lists any information regarding complications.

**Column G** lists any comments made by the authors regarding the study design or other methodological issues.

**Column H** lists the authors' overall conclusions on the use of spinal cord stimulation.

**Column I** is intentionally blank.

**Column J** lists any information given regarding the conduct of a trial period.

**Column K** lists any information given regarding the criteria for judging a trial as successful.

## Appendix 5

The Excel workbook intrathecal drug delivery –primary sources.xls lists all of the original studies referenced by the authors of systematic reviews and evidence-based guidelines.

**Column A** gives the ID#(s) ID# of included in this analysis that referenced this primary source

**Column B** is the citation of the primary source

REPORT TO THE MSRB

*Spinal Cord Stimulators*

September 2, 2008

Received, Reviewed and Adopted by the Medical Services Review Board  
October 23, 2008

The Department has prepared this report spinal cord stimulators in accordance with the guidelines and formats used in the MSRB Charge to its Medications Task Force (October 14, 2004 MSRB meeting). The overall clinical question considered in this review was:

1. What is the proper use of spinal cord stimulators in the treatment of chronic spinal pain and complex regional pain syndrome (reflex sympathetic dystrophy)?

This overall question was addressed by identifying and synthesizing the best available medical data on the following specific issues:

Are spinal cord stimulators *effective* in the treatment of chronic spinal pain and complex regional pain syndrome (reflex sympathetic dystrophy)?

Are spinal cord stimulators *safe*?

What is the appropriate trial period for determining if a patient will have a favorable response to treatment with a spinal cord stimulator?

What are the appropriate criteria for judging whether a patient had a favorable response during a trial period?

### Department Work Plan

The Department used the same “evidence-based medicine” approach to spinal cord stimulators as had been employed by the MSRB’s Medications Task Force in preparing its report on non-steroidal anti-inflammatory drugs (NSAIDs)<sup>1</sup>. Evidence-Based Medicine (EBM) “is the process of systematically reviewing, appraising and using clinical research findings to aid the delivery of optimum clinical care to patients.”<sup>2</sup> EBM replaces clinical intuition, observations from personal clinical experience, and hypothetical arguments based on pathophysiological principles, as the principle grounds for clinical decision-making. Instead evidence from systematic surveys and critical appraisals of peer-reviewed, methodologically-sound clinical research is gathered, reviewed and synthesized using standardized, objective protocols based on agreed rules of evidence.

Key components of the evidence-based medicine approach used by the Department are:

- a) the systematic search for, and retrieval of, all the relevant medical literature regarding the use of spinal cord stimulators that addresses one or more of the specific issues listed above;
- b) sorting the retrieved literature by level of evidence;
- c) critical appraisal of that literature to systematically examine its validity, results and relevance; and,
- d) synthesis of the findings, with a grade of recommendation.

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1 Final Report. MSRB Task Force On Medications. Nonsteroidal Anti-Inflammatory Drugs, July 21, 2005

2 Rosenberg W, Donald A. “Evidence-based medicine: an approach to clinical problem solving” BMJ 1995; 310(6987): 1122–1126

Strauss SE, Richardson WS, Glasziou P, Haynes RB Evidence-based Medicine: How to Practice and Teach EBM Edinburgh; Churchill Livingstone, 2005

The search and retrieval of the medical literature was done using computerized search engines and on-line bibliographical databases of the medical literature. In order to maximize the efficient use of time and resources, the same strategies as used by the MSRB's Medications Task Force in its analysis on NSAIDs were adopted to target the searches to the best and most recent evidence by using a step-wise search process.

First, the Department searched the medical literature by "level of evidence." The levels of evidence (Table 1) are a hierarchy representing the strength of the conclusion that can be drawn from a study of that type. Level I evidence is the most compelling, while Level VI evidence is the weakest. The Department restricted the initial search of the medical literature to Level I evidence – systematic reviews and meta-analyses. A systematic review is itself a review of the medical literature conducted using methods (including systematic search and retrieval of all the relevant primary source evidence and critical appraisal of the evidence found using standardized techniques) designed to minimize the likelihood of bias in the results. A meta-analysis is a systematic review in which quantitative methods are used to summarize the results of the review<sup>3</sup>. Not only are systematic reviews and meta-analyses the strongest evidence available but they have the additional property of representing the other levels of evidence.

Table 1: Levels of Evidence<sup>4</sup>

I	systematic reviews/meta-analyses of multiple randomized, controlled trials
II	randomized, controlled trials
IIIA	controlled studies without randomization
IIIB	other types of quasi-experimental study
IV	non-experimental descriptive studies
V	case series
VI	expert committee reports or opinions/clinical experience of respected authorities, or both

Using Level I evidence means that the Department could review efforts by other researchers who had already searched the medical literature for Level II and higher evidence, retrieved and reviewed these studies to determine their relevance and methodological quality, abstracted and evaluated their findings, and synthesized the results. This allowed the Department to leverage its resources to review a much larger body of evidence.

Second, the Department tried to focus the search on the most recent studies, so as to best represent the most current information.

The Department also searched for any already published, evidence-based guidelines for the use of spinal cord stimulators.

<sup>3</sup> Guyatt G, Rennie D *Users' Guides to the Medical Literature. Essentials of Evidence-Based Clinical Practice* AMA Press, 2002  
FOCUS "Critical Appraisal Tool" at <http://www.focusproject.org.uk/>

<sup>4</sup> Adapted from Phillips B, Ball C, Sackett D, Badenoch D, Straus S, Haynes B, Dawes M "Levels of Evidence and Grades of Recommendation" Oxford Centre for Evidence-based Medicine, 1998 [http://www.cebm.net/levels\\_of\\_evidence.asp](http://www.cebm.net/levels_of_evidence.asp)

Prior to beginning the literature search, the Department adopted a set of guidelines for determining when and how the searches would be extended that were similar to those used by the MSRB's Medications Task Force in its analysis on NSAIDs. If at least 10 valid and unrelated references to systematic reviews were not found, the search would be extended to look for all articles in category II (randomized controlled trials) and for all articles in category I (systematic reviews) in the entire database.

The search for relevant medical literature was in fact extended to all levels of evidence. And the search was extended back in time to encompass all of the available literature in the on-line databases.

The Department conducted the literature searches in two electronic bibliographic databases:

1. Medline through the PubMed portal at <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi> ; and,
2. The Cochrane Library (The Cochrane Database of Systematic Reviews, Database of Abstracts of reviews of Effects, and The Cochrane Central Register of Controlled Trials) through the Lumina portal of the University of Minnesota Libraries at [http://tc.liblink.umn.edu/sfx\\_local/a-z/default](http://tc.liblink.umn.edu/sfx_local/a-z/default).

PubMed is a service of the National Library of Medicine (NLM) available via the National Center of Biotechnology's Entrez retrieval system. PubMed is a public access search engine for MEDLINE, NLM's premier bibliographic database for medical literature. MEDLINE contains bibliographic citations and author abstracts from more than 4,800 biomedical journals published in the United States and 70 other countries. The database contains over 12 million citations dating back to mid-1960.

The Cochrane Library consists of a regularly updated collection of evidence-based medicine databases created by the Cochrane Collaboration, an international non-profit independent organization of health care providers and health care researchers. The Cochrane Library is a collection of evidence-based medicine databases, which is up-dated quarterly from the best available information about healthcare interventions found in both published and unpublished medical studies from around the world. The Cochrane Database of Systematic Reviews (CDSR) is the collection of systematic reviews done by Cochrane Collaboration work groups. The Database of Abstracts of Reviews of Effects (DARE) contains summaries of systematic reviews done by others, which have met strict quality criteria established by the Cochrane Collaboration. Included reviews have to be about the effects of interventions. The Cochrane Central Register of Controlled Trials (CENTRAL) includes details of clinical trials found in bibliographic databases (notably MEDLINE and EMBASE), and other published and unpublished sources.

The Department used the same inclusion criteria used by the MSRB's Medications Task Force in its analysis on NSAIDs to determine which of the studies found in the automated searches would be retrieved for further analysis. First, the title of the article was reviewed to confirm that the article was about the therapeutic use of spinal cord stimulators in humans. The abstracts and bibliographical data were then retrieved for articles meeting the first screening and reviewed to determine if:

- the article addressed one of the specific issues of relevance about spinal cord stimulators;
- the article represented a study of the appropriate level of evidence;
- it was a study published during the search time frame;
- the article was published in English; and
- the article was available on-line through the University of Minnesota Bio-Medical Library.

Articles selected for inclusion after a review of the article abstract were retrieved in electronic format from the University of Minnesota Bio-Medical Library through the Lumina portal. An electronic database was created listing the authors, the title of the article, and the journal reference. Each article's abstract and full text was then hyperlinked to its citation in the database. Retrieved articles were evaluated for their level of evidence and assigned a "relevance" category. Systematic reviews (and/or meta-analyses) and randomized controlled trials were considered to be of "high" relevance. Other types of controlled trials and economic evaluations were considered to be of "medium" relevance. Unsystematic reviews, editorials, case series, case studies and all other types of articles were considered to be of "low" relevance.

An additional computerized search for guidelines, using the key words "pain" and "spinal cord stimulation" was conducted at the websites of organizations known to be active in guideline development, appraisal, or cataloging:

<b>Country</b>	<b>Name of organization</b>	<b>Website</b>
Netherlands	Dutch Institute for Healthcare Improvement	<a href="http://www.cbo.nl">http://www.cbo.nl</a>
New Zealand	New Zealand Guidelines Group	<a href="http://www.nzgg.org.nz">http://www.nzgg.org.nz</a>
	Accident Compensation Corporation	<a href="http://www.acc.co.nz/index.htm">http://www.acc.co.nz/index.htm</a>
Scotland	Scottish Intercollegiate Network	<a href="http://www.sign.ac.uk">http://www.sign.ac.uk</a>
Sweden	Swedish Council on Technology Assessment in Health Care	<a href="http://www.sbu.se">http://www.sbu.se</a>
UK	National Library of Guidelines	<a href="http://www.library.nhs.uk/guidelinesfinder">http://www.library.nhs.uk/guidelinesfinder</a>
USA	National Institutes of Health Consensus Development Program	<a href="http://consensus.nih.gov">http://consensus.nih.gov</a>
	National Guideline Clearinghouse	<a href="http://www.guideline.gov">http://www.guideline.gov</a>
	Agency for Healthcare research & Quality	<a href="http://www.ahrq.gov/">http://www.ahrq.gov/</a>

Finally, the computerized searches were supplemented by hand searches of the bibliographies of key articles (particularly systematic reviews and guidelines) and with articles submitted by interested parties.

Articles chosen for analysis were then assessed for their quality using criteria that were appropriate to the study type.

For systematic reviews, the quality criteria chosen were:

<b>1. Study Identification</b>	
Multiple electronic databases	
Unbiased explicit searching strategies	
Hand searches	
Attempts to include "gray" literature	
Estimation of potential publication bias	
<b>2. Study selection</b>	
Only randomized controlled trials included	
Explicit inclusion/exclusion criteria	
Selection criteria applied uniformly	
Rationale for excluding studies	
<b>3. Appraisal of studies</b>	
Described in detail	
Uniformly applied to all studies	
Important parameters addressed	
<ul style="list-style-type: none"> <li>• random allocation</li> <li>• double blinding</li> <li>• relevant outcome measures</li> <li>• follow-up of at least 80 per cent of participants</li> <li>• analysis consistent with the study design</li> </ul>	<p>---</p> <p>---</p> <p>---</p> <p>---</p> <p>---</p>
Effect of study quality on conclusions assessed	
<b>4. Data Collection</b>	
Was missing information considered?	
<b>5. Data synthesis</b>	
Assessment for heterogeneity	
All valid studies used	
Sensitivity analysis performed	
Variations between studies considered	

For randomized controlled trials, the quality criteria were:

Random allocation	
Minimal dropouts (< 15%)	
Blinding of patient	
Blinding of the assessor	
Co-treatments have been used in an equivalent manner among treatment groups.	
Assessment of the extent of patient adherence to the prescribed therapy	
No unintended crossovers from one study treatment to the other.	
Adequate consideration of statistical and clinical significance of findings.	
Adequate demographic description of patients, including at least age, gender, and referral source.	
Adequate clinical description, including pain duration, neurologic deficits, sciatica, previous surgery, and other inclusion or exclusion criteria.	
Adequate description of treatment in terms of dosage, duration, frequency, and technique.	
Reporting of all relevant outcomes, which may include symptoms, physiologic changes, functional ability, costs of care, and psychological measures.	

These criteria were adapted from recommendations for critical appraisal of systematic reviews and randomized controlled trials found in the peer-reviewed literature and textbooks of evidence-based medicine.<sup>5</sup>

For guidelines, the quality criteria were derived from the instrument developed by The AGREE Collaboration started in 1998 as a research project under the Biomedicine and Health Research (BIOMED 2) Programme, funded by the European Union<sup>6</sup>:

<b>Scope and purpose</b>	
Objective(s) of the guideline are specifically described.	
The clinical question(s) is specifically described.	
The patients to whom the guideline is meant to apply is specifically described.	
<b>Stakeholder involvement</b>	
The guideline development group includes individuals from all the relevant professional groups.	
The patients' views and preferences are sought.	
<b>Rigour of development</b>	
Systematic methods are used to search for evidence.	
The criteria for selecting the evidence are clearly described.	
The methods used for formulating the recommendations are clearly described.	
The health benefits, side effects and risks are considered in formulating the recommendations.	
There is an explicit link between the recommendations and the supporting evidence.	
The guideline was externally reviewed by experts prior to publication.	
A procedure for updating the guideline is provided.	
<b>Clarity and presentation</b>	
The recommendations are specific and unambiguous.	
The different options for diagnosis and/or treatment of the condition are clearly presented.	
Key recommendations are easily identifiable.	
<b>Applicability</b>	
The target users of the guideline are clearly defined.	
The potential organizational barriers in applying the recommendations are discussed.	
The potential cost implications of applying the recommendations were considered.	
The guideline is supported with tools for application.	
The guideline presents key review criteria for monitoring and audit purposes	
The guideline was piloted among end users.	
<b>Editorial independence</b>	
The guideline is editorially independent from the funding body.	
Conflicts of interest of guideline development members are recorded.	

Articles were scored “yes”, “no”, “can’t tell” on each item. A summary score was determined by adding together the “yes” responses, dividing by the total number of criteria. This scoring system is a short hand way of indicating overall study quality and is similar to systems used in many systematic reviews for evaluating primary source literature.

<sup>5</sup> Oxman AD, Cook DJ, Guyatt GH “Users' guides to the medical literature. VI How to use an overview” *Journal of the American Medical Association* 1994; 272(17): 1367-1371

Guyatt GH, Sackett DL, Cook DJ “Users' guides to the medical literature. II. How to use an article about therapy or prevention. A. Are the results of the study valid?” *Journal of the American Medical Association* 1993; 270(21): 2598-601.

Crombie IK *The Pocket Guide to Critical Appraisal: A Handbook for Healthcare Professionals* London; BMJ Publishing Group, 1996

<sup>6</sup> <http://www.agreecollaboration.org/>

In addition, the author's conclusions regarding spinal cord stimulator were abstracted, and, in the case of the systematic reviews, the primary literature relied upon by the author(s) in reaching their conclusions was identified and tabulated. The results of the quality review, the author's conclusions, and, if relevant, the bibliography of the primary source literature were entered into a "Summary Sheet" for each article. These Summary Sheets were then also hyperlinked to the Department database.

Finally, the abstracted conclusions from each article were transferred to a separate spreadsheet. There, the conclusions were first sorted onto different pages based on the clinical population addressed in the study (Failed back Surgery Syndrome (and other spinal pain problems), Complex Regional Pain Syndrome, and Mixed Chronic Pain Patients); then they were arranged thematically into columns for comparison across articles.

## Results

The first PubMed search used a search string published in the medical literature that has been validated as both sensitive and specific for retrieving systematic reviews.<sup>7</sup> The search string was combined first with the key words "spinal cord stimulator" and "neurostimulator." Because a search done limiting articles to those published since 1990 yielded less than 10 unique references, this search was expanded to the entire Pub Med database. Expanding this search to the entire PubMed database still did not yield more than 10 unique references, so the search was eventually expanded to include other types of articles. Separate searches were done for articles reporting on the use of spinal cord stimulator in low back pain patients and in patients with complex regional pain syndrome (reflex sympathetic dystrophy). The results of the searches can be found in the documents "SCS and LBP.doc", "SCS and RSD.doc", "Neurostim and LBP.Doc", "Neurostim and RSD.Doc", "SCS-CT.doc", "SCS-meta\_analysis.doc", and "SCS-RCT.doc" (Available at: <http://www.doli.state.mn.us/msrb/scs/>).

These searches retrieved 161 titles, some found more than once. Of these, 63 articles were presumed relevant based on their title and retrieved for further review.

The searches of the Cochrane Database of Systematic Reviews (CDSR) of the Database of Abstracts of Reviews of Effects (DARE) were done using the key word "spinal cord stimulator" and did not yield any new references not found in the PubMed search.

The hand search added 4 articles which were considered potentially relevant (their ID# marked with a suffix "h" in the database) and 2 articles were submitted by interested parties (their ID# marked with a suffix "s" in the database).

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<sup>7</sup> "(meta-analysis [pt] OR meta-analysis [tw] OR metanalysis [tw]) OR ((review [pt] OR guideline [pt] OR consensus [ti] OR guideline\* [ti] OR literature [ti] OR overview [ti] OR review [ti]) AND ((Cochrane [tw] OR Medline [tw] OR CINAHL [tw] OR (National [tw] AND Library [tw])) OR (handsearch\* [tw] OR search\* [tw] OR searching [tw]) AND (hand [tw] OR manual [tw] OR electronic [tw] OR bibliographi\* [tw] OR database\* OR (Cochrane [tw] OR Medline [tw] OR CINAHL [tw] OR (National [tw] AND Library [tw])))) OR ((synthesis [ti] OR overview [ti] OR review [ti] OR survey [ti]) AND (systematic [ti] OR critical [ti] OR methodologic [ti] OR quantitative [ti] OR qualitative [ti] OR literature [ti] OR evidence [ti] OR evidence-based [ti])) BUTNOT (case\* [ti] OR report [ti] OR editorial [pt] OR comment [pt] OR letter [pt]) " found in Shojania KG, Bero LA. "Taking advantage of the explosion of systematic reviews: an efficient MEDLINE search strategy" *Eff Clin Pract* 2001;4(4): 157-62.

The search for guidelines on the World Wide Web found 9 and another was submitted by an interested party.

References for all the articles chosen for further review were combined in an Excel database, spinal-stim.xls (see Appendix 3). Of the 79 articles (9 systematic reviews, 6 randomized controlled trials, 12 guidelines, 3 clinical trials, 6 economic evaluations, 11 unsystematic reviews/editorials, and 32 case series/studies), the full article was available electronically for 44 of them through the Lumina portal at the University of Minnesota (9 systematic reviews, 5 randomized controlled trials, 2 guidelines, 2 clinical trials, 6 economic evaluations, 6 unsystematic reviews/editorials, and 14 case series/studies). Ten guidelines were available through the World Wide Web or were made available by an interested party. When available, the full article was hyperlinked to the database. The article's abstract was then reviewed to determine level of evidence and the relevance of the article.

In all, 14 articles met the inclusion criteria (9 systematic reviews, 5 randomized controlled trials, 12 guidelines) and were entered into a second Excel database, spinal stim - review.xls (see Appendix 4). A quality review was then performed for each article.

The retrieved articles varied in quality. The systematic reviews had summary quality scores ranging from 5/22 to 20/22. However, 5 of the 7 systematic reviews had quality scores greater than 15/22. The randomized controlled trials had summary quality scores ranging from 8/12 to 10/12. The guidelines had summary quality scores ranging from 7/23 to 20/23; however, 5 had scores greater than 13/23.

Overall, all of the systematic reviews and RCTs addressed the question of effectiveness. Five of the systematic reviews and three of the RCTs addressed issues of safety. Two systematic reviews focused on the use of spinal cord stimulators in patients with low back pain, two focused on their use in patients with complex regional pain syndrome (reflex sympathetic dystrophy) and five assessed the effectiveness of spinal cord stimulators in general. Two RCTs included only patients with low back pain and the others included only patients with complex regional pain syndrome (reflex sympathetic dystrophy). Five of the systematic reviews reported on the criteria used for judging whether a patient had a favorable response during a trial period; four reported on the appropriate trial period.

Three of the guidelines were specific to the use of spinal cord stimulators in patients with complex regional pain syndrome (reflex sympathetic dystrophy); one addressed only use in patients with failed back surgery syndrome, while three addressed their use in chronic pain patients without concern for the underlying condition. The others provided guidance regarding both complex regional pain syndrome (reflex sympathetic dystrophy and failed back surgery syndrome cases. The evidence used in developing the recommendations was referenced in the available text for 10 of the 12 guidelines. Those guidelines all relied, at least in part, on systematic reviews and RCTs; in most cases those systematic reviews and RCTs were the same ones identified in the searches done for this report (as noted in columns K and L of spinal stim - review.xls).

The conclusions made by the article’s author(s) were then abstracted and entered into a third database, spinal stim - analysis.xls (see Appendix 4). There, the conclusions were first sorted onto different pages based on the clinical population addressed in the study (Failed back Surgery Syndrome (and other spinal pain problems), Complex Regional Pain Syndrome, and Mixed Chronic Pain Patients); then they were arranged thematically into columns for comparison across articles. Themes were identified inductively from the abstracted conclusions by arranging them into the fewest mutually exclusive categories.

The themes identified were:

<i>theme</i>	<i># articles</i>	<i>summary quality scores</i>
Sources of data	SysRev: 9 RCT: 5 Guidelines: 10	SysRev: 5/22 – 20/22 RCT: 8/12 – 10/12 Guidelines: 7/23 – 20/23
Comments on data	SysRev: 7 RCT: 5 Guidelines: 10	SysRev: 5/22 – 20/22 RCT: 8/12 – 10/12 Guidelines: 7/23 – 20/23
Quantitative results	SysRev: 9 RCT: 5 Guidelines: 6	SysRev: 5/22 – 20/22 RCT: 8/12 – 10/12 Guidelines: 10/23 – 20/23
Reported complications	SysRev: 6 RCT: 4 Guidelines: 1	SysRev: 5/22 – 18/22 RCT: 9/12 – 10/12 Guidelines: 14/23
Study design issues	SysRev: 7 RCT: 5 Guidelines: 0	SysRev: 5/22 – 20/22 RCT: 8/12 – 10/12
Author’s overall conclusions	SysRev: 8 RCT: 5 Guidelines: 11	SysRev: 5/22 – 20/22 RCT: 8/12 – 10/12 Guidelines: 10/23 – 20/23
Comments on length of trial period	SysRev: 3 RCT: 1 Guidelines: 0	SysRev: 5/22 – 20/22 RCT: 10/12
Comments on judging trial success	SysRev: 3 RCT: 5 Guidelines: 0	SysRev: 5/22 – 20/22 RCT: 8/12 – 10/12

## Conclusions

The Department found considerable agreement of published opinion on each issue. While the individual articles varied in quality, this variation does not significantly affect the conclusions reached by the authors. Articles of higher quality most often reached the same conclusions as those of lower quality.

Nine of the 12 guidelines recommended the use of spinal cord stimulation in at least some clinical situations (5 of 6 guidelines with recommendations for back pain patients; 7 of 8 guidelines with recommendations for complex regional pain syndrome patients; 2 of 3 guidelines for recommendations for chronic pain patients in general).<sup>8</sup> The guidelines not recommending

<sup>8</sup> Some guidelines had recommendations for more than one clinical situation.

the use of spinal cord stimulators did not differ markedly in quality from those recommending their use but did tend to rely on a smaller base of data.

The conclusions drawn by the Department from the reviewed literature are:

1. There is limited evidence (predominantly from case series and two RCTs) that permanently implanted spinal cord stimulators are effective in achieving at least a 50% reduction in pain in 50%- 60% of patients with chronic spinal conditions who have a positive response during a screening trial period.

<u>reference</u>	<u>author's conclusions</u>
<u>Neurosurgery. 1995 Dec;37(6):1088-95</u>	In sum, approximately 50 to 60% of patients with FBSS report $\geq$ 50% pain relief with SCS.
<u>Spine. 2005 Jan 1;30(1):152-60</u>	The level of evidence for the efficacy of SCS in patients with CLBP/FBSS remains "moderate." The greatest level of pain relief following SCS appeared to be associated with case series that were of poor quality, short follow-up duration, undertaken in a multicenter setting, and that recruited patients with CLBP or FBSS specifically.
<u>Neurosurgery. 2005;56(1):98-106</u>	This prospective, randomized trial confirms the inference from previous studies that SCS is superior to reoperation in patients with persistent radicular pain after lumbosacral spine surgery. In patients with persistent radicular pain after lumbosacral spine surgery, therefore, our findings indicate that clinicians should offer SCS as an alternative to repeated operation before exhausting all surgical alternatives.
<u>Pain xxx (2007) xxx-xxx</u>	The favorable effect of SCS on neuropathic pain is consistent with the results of previously reported trials.
<u>Eur Spine J 2006; 15:S192-S300</u>	We cannot recommend the use of spinal cord stimulation for the treatment of chronic nonspecific LBP.
<u>Assessment and management of chronic pain. </u>	Patients with lumbar and cervical radiculopathy who are not surgical candidates, and patients with postlaminectomy syndrome are the best candidates for SCS.
<u>Considered Judgment Form: Neuromodulation-Spinal Cord Stimulation</u>	We do not recommend spinal cord stimulation for the treatment of adults with pain due to failed back surgery syndrome.
<u>Treatment in Workers' Compensation 2006</u>	Recommended only for selected patients in cases when less invasive procedures have failed or are contraindicated, and following a successful temporary trial
<u>J Neurosurg 2004; 100:S254-S67</u>	There is some evidence to indicate that SCS has positive, symptomatic, long-term effects on ... failed-back surgery syndrome pain.
<u>Cochrane Database Syst Rev. 2004;(3):CD003783</u>	At the present time there is limited evidence that spinal cord stimulators are effective for some types of chronic pain (FBSS ...).
<u>J Pain Symptom Manage 2004; 27:370-378</u>	SCS is economically favorable in comparison to other therapies for patients with FBSS.... The initial acquisition costs of SCS appear to be offset by a reduction in healthcare resources, such as drug therapy, physician visits, and hospitalization episodes.
<u>Spinal cord stimulation for the management of pain: recommendations for best clinical practice</u>	For indications strongly supported by evidence, i.e. ..., neuropathic pain following spinal surgery..., SCS should be considered early in the patient's management when simple first line therapies have failed. SCS should not necessarily be considered a treatment of last resort.
<u>Evidence-based clinical practice guideline for interdisciplinary rehabilitation of chronic non-malignant pain syndrome patients</u>	Do not recommend using spinal cord stimulators with chronic pain patients.
<u>Summary and Conclusions of the SBU Report on: Methods of Treating Chronic Pain. A Systematic Review</u>	Spinal cord stimulation has been shown to reduce ... low back (Evidence Grade 2) pain.

2. There is limited evidence (predominantly from case series and one RCT) that permanently implanted spinal cord stimulators are effective in achieving at least a 50% reduction in pain in 50%- 67% of patients with complex regional pain syndrome (reflex sympathetic dystrophy) who have a positive response during a screening trial period.

<u>reference</u>	<u>author's conclusions</u>
<u>Clin J Pain. 2003 Nov-Dec;19(6):371-83</u>	We conclude that available evidence suggests that SCS is effective for

	the management of pain for patients with CRPS who did not respond to more conservative medical management (grade B/C).
<a href="#">Eur J Pain 2006 10(2) 91-101</a>	SCS appears to be an effective therapy in the management of patients with CRPS type I (Level A evidence) and type CRPS II (Level D evidence). Moreover, there is evidence to demonstrate that SCS is a cost-effective treatment for CRPS type I.
<a href="#">N Engl J Med. 2000 Aug 31;343(9):618-24</a>	In carefully selected patients with chronic reflex sympathetic dystrophy, electrical stimulation of the spinal cord can reduce pain and improve health-related quality of life.
<a href="#">Ann Neurol. 2004 Jan;55(1):13-8</a>	We conclude that after careful selection and successful test stimulation SCS is safe and has long-term effectiveness in reducing pain.
<a href="#">N Engl J Med. 2006 Jun 1;354(22):2394-6</a>	The pain-alleviating effect of SCS in CRPS diminishes with time, and is no longer statistically significant after 3 years.
<a href="#">Spinal Cord Stimulation. Use in Patients with Complex Regional Pain Syndrome</a>	Incorporating the lack of high level medical research on this subject, along with its significant potential adverse effect rate and poor compensation outcome measures when SCS are used, the WCB should continue with its present position of not authorizing its use in the injured worker population.
<a href="#">Eur J Neurol 2007; 14:952-970</a>	Level B evidence for effectiveness of SCS in CRPS I
<a href="#">Assessment and management of chronic pain.</a>	Patients with complex regional pain syndrome (CRPS) type I or (RSD) are the best candidates for SCS.
<a href="#">Considered Judgment Form: Neuromodulation-Spinal Cord Stimulation</a>	We recommend spinal cord stimulation should be used in highly selected patients with complex regional pain syndrome type I.
<a href="#">Complex Regional Pain Syndrome type I Guidelines</a>	Pain control with spinal cord stimulation is a responsible choice for carefully selected CRPS-I patients who have not responded to other treatments.
<a href="#">Treatment in Workers' Compensation 2006</a>	Recommended only for selected patients in cases when less invasive procedures have failed or are contraindicated, and following a successful temporary trial
<a href="#">Evidence Based Review. Spinal Cord Stimulation</a>	There is no quality evidence that SCS is superior treatment long term especially when a cost/benefit perspective is required
<a href="#">J Neurosurg 2004; 100:S254-S67</a>	There is some evidence to indicate that SCS has positive, symptomatic, long-term effects on CRPS I and II ...
<a href="#">Cochrane Database Syst Rev. 2004;(3):CD003783</a>	At the present time there is limited evidence that spinal cord stimulators are effective for some types of chronic pain (... CRPS Type 1).
<a href="#">J Pain Symptom Manage 2004; 27:370-378</a>	SCS is economically favorable in comparison to other therapies for patients with ... CRPS. The initial acquisition costs of SCS appear to be offset by a reduction in healthcare resources, such as drug therapy, physician visits, and hospitalization episodes.
<a href="#">Spinal cord stimulation for the management of pain: recommendations for best clinical practice</a>	For indications strongly supported by evidence, i.e. CRPS, ... SCS should be considered early in the patient's management when simple first line therapies have failed. SCS should not necessarily be considered a treatment of last resort.
<a href="#">Evidence-based clinical practice guideline for interdisciplinary rehabilitation of chronic non-malignant pain syndrome patients</a>	Do not recommend using spinal cord stimulators with chronic pain patients.
<a href="#">Summary and Conclusions of the SBU Report on: Methods of Treating Chronic Pain. A Systematic Review</a>	Spinal cord stimulation has been shown to reduce peripheral neuropathic (Evidence Grade 3) ... pain. Notwithstanding high initial expenses, spinal cord stimulation combined with physical therapy is cost-effective in treating neuropathic pain (Evidence Grade 3).

3. There is inconsistent evidence as to whether spinal cord stimulators improve other clinical outcomes in patients with either chronic spinal conditions or complex regional pain syndrome (reflex sympathetic dystrophy).

<i>reference</i>	<i>author's conclusions</i>
<a href="#">Neurosurgery. 1995 Dec;37(6):1088-95</a>	However, there is insufficient evidence to draw conclusions ... about the effects of SCS on patient work status, functional disability, and health care and medication use.
<a href="#">Clin J Pain. 2003 Nov-Dec;19(6):371-83</a>	Definitive conclusions cannot be made with regard to any of the secondary outcome measures, in part due to poor methodological design and in part due to inadequate reporting by the authors.
<a href="#">Spinal Cord Stimulation. Use in Patients with Complex Regional Pain Syndrome</a>	Incorporating the lack of high level medical research on this subject, along with its significant potential adverse effect rate and poor compensation outcome measures when SCS are used, the WCB should continue with its present position of not authorizing its use in the

	injured worker population.
<u>Pain. 2004 Mar;108(1-2):137-47</u>	We conclude that the literature on SCS for FBSS ... remains inadequate to make definitive statements about efficacy in reducing physical disability, work disability, and medication consumption.

4. There is inconsistent evidence as to whether spinal cord stimulators are more effective than alternatives for relieving pain in patients with either chronic spinal conditions or complex regional pain syndrome (reflex sympathetic dystrophy).

<i>reference</i>	<i>author's conclusions</i>
<u>Neurosurgery. 1995 Dec;37(6):1088-95</u>	No conclusions may be drawn concerning the efficacy of SCS for FBSS relative to other treatments, placebo treatments, or no treatment.
<u>N Engl J Med. 2006 Jun 1;354(22):2394-6</u>	The pain-alleviating effect of SCS in CRPS diminishes with time, and is no longer statistically significant after 3 years.
<u>Complex Regional Pain Syndrome type 1 Guidelines</u>	Pain control with spinal cord stimulation is a responsible choice for carefully selected CRPS-I patients who have not responded to other treatments.
<u>Treatment in Workers' Compensation 2006</u>	Recommended only for selected patients in cases when less invasive procedures have failed or are contraindicated, and following a successful temporary trial
<u>Evidence Based Review. Spinal Cord Stimulation</u>	There is no quality evidence that SCS is superior treatment long term especially when a cost/benefit perspective is required
<u>Pain. 2004 Mar;108(1-2):137-47</u>	Using recently published criteria for levels of evidence, there is moderate evidence (one high-quality RCT) that SCS plus PT is more effective than PT-only for patients with CRPS type I in relieving pain at 6- and 12-month follow-ups. Both the RCT and lower-quality studies suggest a modest pain-relieving effect on average. Less regarding comparisons with placebo controls, other treatments, or the natural history can be gleaned from the literature.

5. Complications occur in 1/3 to 1/2 of cases, but are often mild and mostly involving problems with the equipment or local infection. But up to 1/3 of patients will require re-operation in the first two years due to complications.

<i>reference</i>	<i>complications</i>
<u>Neurosurgery. 1995 Dec;37(6):1088-95</u>	<ul style="list-style-type: none"> <li>o 13 studies: 42% (range 20-75%) of patients had some kind of complication.</li> <li>o 20 studies: 5% (range 0-12%) of patients had an infection.</li> <li>o 17 studies: 9% (range 0-42%) of patients had a biological complication other than infection.</li> <li>o 13 studies: 30% (range, 0-75%) of patients had one or more stimulator-related complications.</li> </ul>
<u>Spine. 2005 Jan 1;30(1):152-60</u>	<ul style="list-style-type: none"> <li>o <u>RCT</u>: Four (17%) and six (26%) patients with FBSS experienced complications at 6 and 12 months post SCS implantation, respectively.</li> <li>o <u>Case Series</u>: Overall, 43% of patients with CBLP/FBSS experienced one or more complications with SCS. The majority of these complications were due to electrode or lead problems (195/722; 27%). Infections (6%), generator problems (6%), extension cable problems (10%), or other issues, such as cerebrospinal fluid leaks (7%), accounted for the remainder.</li> </ul>
<u>Neurosurgery. 2005;56(1):98-106</u>	One SCS patient developed an infection at the receiver site, which was treated by removal of the system followed by specific antibiotic therapy. The system was replaced without further complication. Three SCS patients (9% of permanent implants) underwent hardware revisions because of technical problems (electrode migration or malposition).
<u>Pain xxx (2007) xxx-xxx</u>	Of 84 patients, 27 (32%) experienced a total of 40 device-related complications. For 20 patients (24%), surgery was required to resolve the event. Principal complications were electrode migration (10%), infection or wound breakdown (8%), and loss of paresthesia (7%).
<u>Pain Physician. 2007 Jan;10(1):7-111</u>	Complications with spinal cord stimulation range from infection, hematoma, nerve damage, lack of appropriate paresthesia coverage,

	paralysis, nerve injury, and death.
<a href="#">Clin J Pain. 2003 Nov-Dec;19(6):371-83</a>	<ul style="list-style-type: none"> <li>o The proportion of patients with at least one complication ranged from 9% to 50%.</li> <li>o The infection rate ranged from 1.4% to 11.1%.</li> <li>o The rate of complication due to technical problems such as equipment failure, lead migration, or lost coverage ranged from 8.3% to 42.8%.</li> <li>o The rate of reoperation ranged from 11.1% to 50%.</li> </ul>
<a href="#">Eur J Pain 2006 10(2) 91-101</a>	<ul style="list-style-type: none"> <li>o <b>RCT:</b> Six of the 36 patients receiving SCS plus physical therapy experienced complications (n = 11) at 6 months but only one complication (infection) was reported at 12 months. A total of 9 of the 24 patients (38%) experienced 22 complications needing operation during the 2-years after implantation.</li> <li>o <b>Case Series:</b> Overall, in eight studies, 33.0% (22/66) of patients reported at least one complication with SCS. The majority of complications were related to electrode issues (20% of patients), infections (4% of patients), generator issues (2% of patients) or extension cable issues (1%) of patients. A further 6% of patients had other complications such as hematomas.</li> </ul>
<a href="#">N Engl J Med. 2000 Aug 31;343(9):618-24</a>	Six of the 24 patients had complications that required additional procedures, including removal of the device in 1 patient.
<a href="#">Ann Neurol. 2004 Jan;55(1):13-8</a>	<p>Four of the six had long term complications.</p> <ul style="list-style-type: none"> <li>o 9 of 24 patients (38%) suffered 22 complications needing operation during the 2 years after implantation.</li> <li>o The most frequent complications were electrode displacement and pain from the pulse generator pocket.</li> <li>o Two patients underwent permanent removal of the system on the grounds of recurrent rejection and relapsing ulcerative colitis subscribed to the system, respectively</li> <li>o Side effects were reported by all 22 patients who still had an implanted system at 2 years.</li> </ul>
<a href="#">Pain Physician. 2007 Jan;10(1):7-111</a>	Complications with spinal cord stimulation range from infection, hematoma, nerve damage, lack of appropriate paresthesia coverage, paralysis, nerve injury, and death.
<a href="#">J Neurosurg 2004; 100:S254-S67</a>	Most complications were not life threatening and could usually be resolved by removing the device. The most common complication was lead migration. The most serious complication was paralysis
<a href="#">Pain. 2004 Mar;108(1-2):137-47</a>	18 articles: average of 34% (range 0–81%) of the patients who received a permanent stimulator had one or more undesirable outcomes during the study follow-up period. These included superficial and deep infections, local pain in the region of stimulator components, biological complications other than infection or local pain (e.g. dural puncture), equipment failure, a stimulator revision (additional operation to correct an equipment problem; we did not include battery changes in this category), and stimulator removal (most commonly because of infection, equipment failure, or lack of pain relief). Removals included both permanent removals and removals followed by eventual re-implantations (e.g. removal due to infection and stimulator implantation after resolution of the infection).

6. Trial screening periods in the reported case series and clinical trials have lasted from 1 day up to 30 days, with most lasting from 3 to 7 days. There is no information to judge whether the length of the trial period influences the reported efficacy of spinal cord stimulation.

<i>reference</i>	<i>trial period</i>
<a href="#">Neurosurgery. 1995 Dec;37(6):1088-95</a>	In 34 studies, there were temporary electrode trials, lasting 1 to 3 days in 4 studies, 4 to 7 days in 8 studies, 8 to 14 days in 4 studies, and more than 2 weeks in 2 studies. The length of the trial considerably varied across patients in 1 study and was not specified in 15 studies.
<a href="#">Neurosurgery. 2005;56(1):98-106</a>	SCS treatment began with percutaneous placement of a temporary electrode for a therapeutic trial lasting at least 3 days.
<a href="#">Clin J Pain. 2003 Nov-Dec;19(6):371-83</a>	Eleven studies reported the duration of the stimulation trial period that ranged from 3 to 30 days. Six of these studies reported trial stimulation

	that lasted 7 days or less. The remaining 5 studies reported trial stimulation of greater than 7 days.
Cochrane Database Syst Rev. 2004;(3):CD003783	1 of 2 studies: Percutaneous placement of a temporary electrode for routine 2- 1/2 day trial.

7. The most common measure of success in the trial period was relief of pain and the most common criteria was pain relief of at least 50%.

<u>reference</u>	<u>trial success</u>
Neurosurgery. 1995 Dec;37(6):1088-95	In the 34 studies in which patients were screened with temporary electrodes to determine suitability for permanent implants, the criteria for permanent implants were specifically stated to be pain relief in 19 studies, region of paresthesia in 8 studies, decreased medication use in 2 studies, and increased activity in 2 studies. Only eight articles stated a threshold percentage of pain relief for permanent implantation, and across these studies, the minimum percent pain relief for implantation ranged from 30 to 75% (30% in one study, 50% in five, 70% in one, and 75% in one).
Neurosurgery. 2005;56(1):98-106	The SCS patients could receive a permanent implant if they reported at least 50% estimated relief of pain by standard pain rating methods and demonstrated stable or improved analgesic medication intake, with improved physical activity commensurate with neurological status and age.
Pain xxx (2007) xxx-xxx	Criteria for implanting SCS: at least 80% overlap of pain distribution with stimulation-induced paresthesia and at least 50% leg pain relief.
Clin J Pain. 2003 Nov-Dec;19(6):371-83	There was considerable variability in the criteria used to determine successful trial stimulation. Quantitative and validated measures of pain relief were not used by all studies to determine trial success. A 50% decrease in VAS score for pain or a rating of 6 on the global perceived effect (GPE) scale was necessary to define success in 2 studies. Three studies used 50% pain relief from baseline VAS scores, while 1 study used walking distance along with 70% pain relief as the primary outcome measure. Other studies used nonspecific outcomes such as "patient satisfied", "acceptable degree of analgesia", "patient benefited", or "pain relief to avoid heavy analgesic use."
N Engl J Med. 2000 Aug 31;343(9):618-24	The decision to implant the permanent SCS system was made when pain intensity during the testing period was at least 50% lower as compared with the original (baseline) visual analog score, or if "much improvement" was reported on a seven-point global perceived effect scale.
Cochrane Database Syst Rev. 2004;(3):CD003783	1 of 2 studies: If a patient reports at least 50% estimated relief of pain, while demonstrated stable or improved medication intake, and improved physical activity commensurate with neurologic status and age, a permanent implant was offered.

## Recommendations

Based on the conclusions derived from the literature the Department proposes the following draft recommendations to the Medical Services Review Board, to be used as the basis for changes to the Permanent Treatment Parameters governing the use of spinal cord stimulators in workers' compensation claims.

**I. Spinal cord stimulators can effectively relieve pain in some patients with chronic spinal pain or complex regional pain syndrome (reflex sympathetic dystrophy).**

**II. An adequate trial period of at least three days is needed to determine who might benefit from spinal cord stimulation.**

**III. Adequate pain relief of at least 50% during the trial period is needed to determine if a patient might benefit from spinal cord stimulation.**

## **Appendix 1**

The Word files "SCS and LBP.doc", "SCS and RSD.doc", "Neurostim and LBP.Doc", and "Neurostim and RSD.Doc", "SCS-CT.doc", "SCS-meta analysis.doc", "SCS-RCT.doc" list all of the articles found in the literature searches.

## Appendix 2

The Excel workbook spinal-stim.xls lists all of the articles that were selected by the Department for further review.

**Column A** is an ID number

**Column B** lists the authors of the article.

**Column C** is the title of the article.

**Column D** gives the abbreviated citation as found in Medline and is an active link.

Clicking on the journal citation will call up the abstract and/or article

**Column E** identifies the type of article:

“SysRev” is a systematic review,

“RCT” is a randomized controlled trial

“CT” is a nonrandomized trial

“CE” is an economic evaluation

“Guide” is an evidence-based treatment guideline

“Review” is an unsystematic review

“Editorial” is a statement of a single physician’s opinion

“CaseSer” is a case series

“CaseRep” is a single case report

**Column F** indicates whether the article was determined to be relevant for the purposes of this study based on the levels of evidence hierarchy.

**Column G** indicates the availability of the article.

**Column H** indicates the patient subgroup(s) discussed in the article.

### **Appendix 3**

The Excel workbook spinal stim - review.xls lists the results of the quality review of the articles that were selected by the Department for this analysis.

**Column A** is an ID number

**Column B** lists the authors of the article.

**Column C** gives the abbreviated citation as found in Medline and is an active link.

Clicking on the journal citation will call up the abstract and/or article

**Column D** identifies the type of article:

“SysRev” is a systematic review,

“RCT” is a randomized controlled trial

“Guide” is an evidence-based treatment guideline.

**Column E** is marked with an “X” if the article discusses efficacy.

**Column F** is marked with an “X” if the article discusses safety.

**Column G** indicates the patient subgroup(s) discussed in the article.

**Column H** is a hyperlink to the summary sheet for the article

**Column I** is the summary quality score of the article

**Column J** includes any comments about the article

***For guidelines only:***

**Column K** lists the ID# for any systematic reviews included in this analysis that were used by the authors of the guideline.

**Column L** lists the ID# for any randomized clinical trials included in this analysis that were used by the authors of the guideline.

**Column M** lists the ID# for any guidelines included in this analysis that were used by the author's of the guideline.

## Appendix 4

The Excel workbook spinal stim -analysis.xls lists the author's findings and conclusions regarding the efficacy and safety of spinal cord stimulators, and any other information relevant to the questions posed for this analysis. Wherever possible, the conclusions are stated in the authors' own words.

This workbook has 3 spreadsheets or pages:

The first page lists the results for articles that addressed the use of spinal cord stimulators in patients with low back pain.

- Column A** gives the abbreviated citation as found in Medline and is an active link. Clicking on the journal citation will call up the abstract and/or article
- Column B** identifies the type of article: "SR" is a systematic review, "RCT" is a randomized controlled trial, and "Guide" is an evidence-based treatment guideline.
- Column C** lists the sources of information used.
- Column D** lists any comments made by the authors regarding the sources of information.
- Column E** lists the quantitative results of the study.
- Column F** lists any information regarding complications.
- Column G** lists any comments made by the authors regarding the study design or other methodological issues.
- Column H** lists the authors' overall conclusions on the use of spinal cord stimulation.
- Column I** is intentionally blank.
- Column J** lists any information given regarding the conduct of a trial period.
- Column K** lists any information given regarding the criteria for judging a trial as successful.

The second page lists the results for articles that addressed the use of spinal cord stimulators in patients with complex regional pain syndrome.

- Column A** gives the abbreviated citation as found in Medline and is an active link. Clicking on the journal citation will call up the abstract and/or article
- Column B** identifies the type of article: "SR" is a systematic review, "RCT" is a randomized controlled trial, and "Guide" is an evidence-based treatment guideline.
- Column C** lists the sources of information used.
- Column D** lists any comments made by the authors regarding the sources of information.
- Column E** lists the quantitative results of the study.
- Column F** lists any information regarding complications.
- Column G** lists any comments made by the authors regarding the study design or other methodological issues.
- Column H** lists the authors' overall conclusions on the use of spinal cord stimulation.
- Column I** is intentionally blank.
- Column J** lists any information given regarding the conduct of a trial period.
- Column K** lists any information given regarding the criteria for judging a trial as successful.

The third page lists the results for articles that addressed the use of spinal cord stimulators in chronic pain patients in general.

**Column A** gives the abbreviated citation as found in Medline and is an active link.

Clicking on the journal citation will call up the abstract and/or article

**Column B** identifies the type of article: “SR” is a systematic review, “RCT” is a randomized controlled trial, and “Guide” is an evidence-based treatment guideline.

**Column C** lists the sources of information used.

**Column D** lists any comments made by the authors regarding the sources of information.

**Column E** lists the quantitative results of the study.

**Column F** lists any information regarding complications.

**Column G** lists any comments made by the authors regarding the study design or other methodological issues.

**Column H** lists the authors’ overall conclusions on the use of spinal cord stimulation.

**Column I** is intentionally blank.

**Column J** lists any information given regarding the conduct of a trial period.

**Column K** lists any information given regarding the criteria for judging a trial as successful.

## Appendix 5

The Excel workbook spinal stim –primary sources.xls lists all of the original studies referenced by the authors of systematic reviews and evidence-based guidelines.

**Column A** gives the ID#(s) ID# of included in this analysis that referenced this primary source

**Column B** is the citation of the primary source