Non-steroidal Anti-inflammatory Drugs (NSAIDs) Subcommittee Report

Update #1, August 2003

This report is an update of the initial NSAIDs Subcommittee Report of June 2002. All revisions are highlighted.

Produced by:
Health Resources Commission
Kathleen Weaver, MD, Director
Office for Oregon Health Policy & Research
255 Capitol Street NE
Salem, OR 97310
Overview for Update #1

The 2001 session of the Oregon Legislature passed Senate Bill 819, authorizing the creation of a Practitioner-Managed Prescription Drug Plan. Statute specifically directs the Health Resources Commission (HRC) to advise the Department of Human Services on this Plan.

In January of 2002 the HRC appointed a subcommittee to perform an evidence-based review of the use of non-steroidal anti-inflammatory drugs (NSAIDs). Members of the subcommittee consisted of physicians, pharmacists, physician assistants, nurse practitioners, other health care professionals, consumers and advocates. The subcommittee had seven meetings, two of which were general sessions of orientation and evidence based analysis education. All meetings were held in public with appropriate notice provided.

Subcommittee members worked with Oregon Health and Science University’s Evidence-based Practice Center (OHSU-EPC) to develop and finalize key questions for drug class review, specifying patient populations, medications to be studied and outcome measures for analysis, considering both effectiveness and safety. Evidence was specifically sought for subgroups of patients based on race, ethnicity, age, demographics, other medications and co-morbidities.

Using standardized methods, the OHSU-EPC reviewed systematic databases, the medical literature and dossiers submitted by pharmaceutical manufacturers. Inclusion and exclusion criteria were applied to titles and abstracts, and each study was assessed for quality according to predetermined criteria.

The OHSU-EPC’s Draft “Drug Class Review on Non-steroidal Anti-inflammatory Drugs” was completed the week of April 29, 2002, circulated to subcommittee members and posted on the web. The subcommittee met on May 6 and May 13, 2002 to review the document and any additional evidence. By consensus, the subcommittee members agreed to adopt the EPC report. Time was allotted for public comment, questions and testimony. The subcommittee’s final meeting was a teleconference on May 20, 2002 to review and approve the subcommittee report to be submitted to the HRC. All available sources of information, EPC report, which includes information submitted by pharmaceutical manufacturers, and public testimony were considered. The conclusions drawn by the NSAIDs Subcommittee comprise the body of this report.

In January of 2003 the HRC appointed an update committee to perform an evidence-based review of the June 2002 Non-steroidal Anti-inflammatory Drugs (NSAIDs) Subcommittee Report for new information or changes in the FDA package inserts. Members of the Update Committee consisted of one HRC member, one OSU pharmacist, one Oregon Health Policy and Research (OHPR) physician, one OHSU-EPC pharmacist, and two NSAIDS Subcommittee
The committee had two meetings held in public with appropriate notice provided. **This report is an update of the initial June 2002 Subcommittee Report. All revisions are highlighted.**

The NSAID Update Committee members worked with the OHSU-EPC reviewing the evidence for both effectiveness and safety. Evidence was specifically sought for differences among subgroups of patients based on race, ethnicity, age, demographics, other medications and co-morbidities.

The OHSU EPC’s draft report, *Drug Class Review on NSAIDs Update Report* was completed May 12, 2003, circulated to committee members and posted on the OHPR website at www.ohpr.state.or.us. The update committee met on May 27, 2003, to review the document and additional evidence. By consensus, the committee members agreed to adopt the EPC report. Time was allotted for public comment, questions, written and oral testimony. All available sources of information from the EPC’s report that included information submitted by pharmaceutical manufacturers and public testimony, were considered. The NSAIDs Update Committee reconvened the original Subcommittee on August 14, 2003 to review changes recommended by the Update Committee. Time was allotted for public comment, questions, written and oral testimony.

This report is prepared to facilitate the HRC in providing recommendations to the Department of Human Services for the plan drug list (PDL). This update report does not recite or characterize all the evidence that was discussed by the OHSU EPC, the NSAIDs Update Committee, the NSAIDs Subcommittee, or the HRC. For further information provided during the committee process, readers are encouraged to review the source materials on the website.

The NSAIDs Update Committee of the HRC, working together with the EPC, Oregon Medical Assistance Program (OMAP), and the OSU College of Pharmacy, will continue to monitor medical evidence for new developments in this drug class. Approximately every six months emerging pharmaceuticals will be reviewed and if appropriate, a recommendation for inclusion in the PDL will be made. Significant new evidence for pharmaceuticals already on the PDL will be assessed and Federal Drug Administration (FDA) changes in indications and safety recommendations will be evaluated. The NSAIDs Subcommittee Report will be amended if indicated. Substantive changes will be brought to the attention of the HRC who may choose to approve the report, or reconvene the NSAIDs Subcommittee.

This report and the OHSU-EPC’s draft update report, *Drug Class Review on NSAIDs*, are available on the Office for Oregon Health Policy & Research, Practitioner-Managed Prescription Drug Plan website: www.oregonrx.org. Information regarding the Oregon Health Resources Commission and its subcommittee policy and process can be found on the OHPR website:
www.ohpr.state.or.us. You may also request more information or minutes and tapes from committee meetings from:

Kathleen Weaver, MD  
Director, Health Resources Commission  
Office for Oregon Health Policy & Research  
255 Capitol St. NE, 5th Floor  
Salem, Oregon 97310  
503-378-2422 ext. 406  
Kathy.weaver@state.or.us

Information dossiers submitted by pharmaceutical manufacturers are available upon request from the OHSU-EPC by contacting:

Jeani Crichlow  
Oregon Health & Science University  
Mailcode: BICC  
3181 SW Sam Jackson Park Road  
Portland, OR 97201-3098  
Phone: 503-494-4502  
Fax: 503-494-4551  
crichlow@ohsu.edu

There will be a charge for copying and handling in providing documents both from the Office for Oregon Health Policy & Research and from OHSU.

**Critical Policy:**

- **Senate Bill 819**
  - “The Department of Human Services shall adopt a Practitioner-managed Prescription Drug Plan for the Oregon Health Plan. The purpose of the plan is to ensure that enrollees of the Oregon Health Plan receive the most effective prescription drug available at the best possible price.”

- **Health Resources Commission**
  - “Clinical outcomes the most important indicators of comparative effectiveness;
  - “If evidence is insufficient to answer a question, neither a positive nor a negative association can be assumed.”

**Inclusion Criteria:**

- **Scope**
- Patients with chronic pain due to osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, soft tissue pain, or back pain. Pain from dysmenorrhea and acute pain, such as from dental procedures and surgery, were excluded. Treatment to prevent development of colorectal polyps was also excluded.

**Efficacy**
- The main efficacy measures are pain, functional status, and discontinuations due to lack of efficacy. Measures vary among studies.

**Safety and Adverse Effects**
- Serious GI events (GI bleeding, symptomatic ulcer disease, perforation of the GI tract, and death).
- GI symptoms (abdominal pain, heartburn, upset stomach)
- Serious cardiovascular events (myocardial infarction, angina, stroke, transient ischemic attack, cardiovascular death, and related measures).
- Tolerability and adverse events including discontinuation due to any adverse effects, the overall rate of adverse events, the rate of GI adverse events, and the combined rate of adverse events related to renal and cardiovascular function, including increased creatinine, edema, hypertension, or congestive heart failure. Frequency of, and discontinuations due to, abnormal laboratory tests, primarily elevated transaminases (liver tests) was also recorded.

**Exclusions:**
- Endoscopic ulcer
- Aseptic meningitis

**Drugs:**

- **COX-2 inhibitors**
  - Celecoxib (Celebrex)
  - Rofecoxib (Vioxx)
  - Valdecoxib (Bextra)

- **COX-2 preferential NSAIDs**
  - Meloxicam (Mobic)
  - Nabumetone (Relafen; others)
- Etodolac (Lodine; others)
- Salsalate (Salflex)

**Non-selective NSAIDs**
- Naproxen (Naprosyn)
- Diclofenac (Voltaren; Cataflam)
- Ibuprofen (Motrin; Advil; others)
- Multiple others

**Key Questions:**

1. In head-to-head comparisons, are there differences in efficacy or safety among different COX-2 inhibitors?

2. Are there differences in efficacy among COX-2 inhibitors, COX-2 preferential NSAIDs, and non-selective NSAIDs?

3. Are there clinically important differences in safety or adverse effects among COX-2 inhibitors, COX-2 preferential NSAIDs, non-selective NSAIDs, and the combination of a non-selective NSAID plus anti-ulcer medication?

4. Are there subgroups of patients based on demographics, other medications, or comorbidities for which one medication is more effective or associated with fewer adverse effects?

**New Findings, 6/03**

- The EPC received dossiers from four pharmaceutical manufacturers for celecoxib, mefenamic acid, rofecoxib and valdecoxib. This information was added to the material identified in our update search.

- Kathy Ketchum, RPh, OSU College of Pharmacy reported no additional drugs, but that the FDA has revised it’s labeling of existing NSAIDs as of August 2002.
  - Based on the CLASS study of 4000 patients where celecoxib 400 mg BID was compared to usual maximal dose of ibuprofen or diclofenac, there was no safety advantage of celecoxib over either ibuprofen or diclofenac.
  - Drug labels should continue to warn doctors and their patients about all NSAIDs for risks of GI ulceration, bleeding and perforation.
- Despite the twice higher than recommended dose of celecoxib, the rates of cardiovascular adverse events were no higher in celecoxib treated patients compared to ibuprofen or diclofenac treated patients.
- The geriatric section of the label will include new information about the risk of serious GI and renal effects in the elderly.

□ Using the same search strategy that was used in the original NSAID report, the EPC found 360 new citations. In addition the Cochrane Review for celecoxib and rofecoxib were updated in August 2002. Of these, approximately 20 were new meta-analyses, systematic reviews, controlled trials or cohort studies on the efficacy or safety of Cox-2 inhibitors.

□ The SUCCESS-7 trial published in November 2002 found higher rates of edema and hypertension for rofecoxib than for celecoxib in patients taking various anti-hypertensive drugs. A new head-to-head trial found no difference between celecoxib, rofecoxib, and ibuprofen in efficacy for acute pain in the emergency department setting. A recently published trial demonstrates that valdecoxib and naproxen have similar efficacy.

□ There was no statistical difference between celecoxib and the combination of diclofenac plus omeprazole over six months in the rate of recurrent ulcer bleeding, but celecoxib was preferable over this combination as far as renal adverse events.

□ The meta-analysis by Mukherjee described in our original report has been criticized by peer review for methodologic flaws, thus removing the conclusion that rofecoxib and celecoxib were associated with higher rates of heart attacks.

□ A meta-analysis of the FDA data from the VIGOR (rofecoxib) and CLASS (celecoxib) trials found a statistical difference in serious adverse events other than GI bleeding that was not explained solely by the increase in cardiovascular events that occurred in the VIGOR trial.

Amended Summary of Results (Changes highlighted)

Comparative Efficacy

1. IN HEAD-TO-HEAD COMPARISONS, ARE THERE DIFFERENCES IN EFFICACY OR SAFETY AMONG DIFFERENT COX-2 INHIBITORS?

Six randomized, multicenter, fair-to-good quality trials directly compared the COX-2 inhibitors celecoxib and rofecoxib. Results were inconsistent amongst the studies.
In two of the trials baseline characteristics were similar but there were discrepancies in history of ulcers, non-specific gastrointestinal symptoms and gender. Discontinuation rates for efficacy for either celecoxib or rofecoxib were similar. In the first, no difference in efficacy of celecoxib and rofecoxib was found, but rofecoxib was found to have statistically significant gastrointestinal adverse effects. In the second, although it was reported that rofecoxib was more effective, re-analysis suggests it was not, and no differences in adverse events were found. Differences between the frequency of adverse events in the two studies may be related to differing baseline incidence of previous GI disease, or due to the fact that one study permitted the use of aspirin and the other did not. The third study focused on renal effects comparing celecoxib and rofecoxib in patients over age sixty-five. Rofecoxib treated patients had a higher rate of edema and a statistically significant increase in systolic blood pressure compared to celecoxib. Non-equivalent dosing may have played a role in frequency of adverse effects.

There are two new studies of elderly patients with hypertension treated with COX-2 inhibitors, but the results are conflicting.

The subcommittee agrees by consensus that evidence comparing celecoxib and rofecoxib is inconsistent and inconclusive and there were no comparison studies including valdecoxib. Current evidence does not support the conclusion that there are differences in either efficacy or safety among COX-2 inhibitors.

2. ARE THERE DIFFERENCES IN EFFICACY AMONG COX-2 INHIBITORS, COX-2 PREFERENTIAL NSAIDS AND NON-SELECTIVE NSAIDS?

a. Celecoxib vs. non-selective NSAIDs

Ten trials comparing celecoxib and non-selective NSAIDs were identified, not all were fully published in peer-reviewed literature. All were short term. Two trials found celecoxib and naproxen to be equally effective. An unpublished trial, raising the concern of publication bias, found naproxen to be superior. In a large study (CLASS) focused largely on adverse effects a higher proportion of NSAIDS patients withdrew for lack of efficacy. In another, no differences were found between celecoxib and ketoprofen.

Of the seven published trials one was rated fair-to-poor, the others were rated good quality. The published trials provide good overall evidence that celecoxib is equivalent to non-selective NSAIDs in efficacy for osteoarthritis and rheumatoid arthritis. One meta-analysis of trials of celecoxib versus
NSAIDs focused on efficacy in elderly patients. Celecoxib 200 mg and 400 mg and naproxen 1000 mg were similar in efficacy.

b. **Rofecoxib vs. non-selective NSAIDs**

Published trials provide good overall evidence that rofecoxib is equivalent to non-selective NSAIDs in efficacy for osteoarthritis. One large, good-quality trial indicates that rofecoxib is equivalent to non-selective NSAIDs in efficacy for rheumatoid arthritis.

c. **Valdecoxib vs. non-selective NSAIDs**

In clinical trials submitted to the FDA, valdecoxib was as effective as ibuprofen, diclofenac and naproxen. One published trial found no difference in efficacy between valdecoxib and naproxen.

d. **COX-2 inhibitor vs. COX-2 preferential NSAID**

One short-term fair-quality multicenter trial compared the efficacy of two different doses of rofecoxib to nabumetone in elderly patients. The rates of not completing the trial were similar. There were no differences between the two doses of rofecoxib and nabumetone in symptom relief. Adverse events could not meaningfully be assessed.

e. **COX-2 preferential vs. non-selective NSAID**

In double-blinded trials of a COX-2 preferential NSAID (meloxicam) versus non-selective NSAIDs, generally no differences in efficacy could be demonstrated. In two trials, patients taking non-selective NSAIDs were significantly less likely to withdraw due to lack of efficacy.

f. **Non-selective NSAID vs. non-selective NSAID**

Several recent good-quality systematic reviews by the Cochrane Collaboration found no clear differences among non-selective NSAIDs in efficacy. COX-2 inhibitors were not included.

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The subcommittee agrees by consensus that evidence does not demonstrate any difference in efficacy among non-selective NSAIDs, COX-2 preferential NSAIDs and COX-2 inhibitors.

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3. **Are there clinically important differences in safety or adverse effects among COX-2 inhibitors, COX-2-preferential NSAIDs, non-selective NSAIDs, or the combination of a non-selective NSAID plus anti-ulcer medication?**
Significant GI events (GI bleeding, hospitalization for GI bleeding, symptomatic ulcer disease, perforation of the GI tract, and death)

3.1 SIGNIFICANT GASTROINTESTINAL EVENTS

a. COX-2 inhibitors

Two trials rated good quality evaluating peptic ulcer disease complications (confirmed complicated event: perforation, obstruction or bleed) were identified. The first (CLASS) compared celecoxib with ibuprofen and diclofenac; the second (VIGOR) rofecoxib versus naproxen.

CLASS found no statistically significant reduction in serious complicated upper GI events. If symptomatic ulcers were included, celecoxib was superior. A post-hoc analysis that stratified patients as to whether they were taking low-dose aspirin prophylaxis for cardiac protection showed celecoxib to be superior for the composite end-point in patients not taking aspirin. For patients taking aspirin the benefit of celecoxib was obviated.

A meta-analysis of celecoxib versus placebo or non-selective NSAIDs with the endpoint of “UGI (upper gastrointestinal) ulcer complications” was identified. Quality of the trials was not assessed. There were fewer upper gastrointestinal ulcer complications in the celecoxib group compared to non-selective NSAIDs and none in the placebo group. This meta-analysis underestimated the risk of ulcer complications with celecoxib. Patients were treated with low-dose celecoxib and the studies were of short duration.

A second study (VIGOR) compared rofecoxib to naproxen. The primary endpoint was a composite of symptomatic ulcer and serious gastrointestinal bleeds. It included older patients compared to CLASS. Results indicated rofecoxib was superior to naproxen with a number needed-to-treat (NNT) to prevent a complicated ulcer-related event of 268, and for the composite endpoint of 191.

Rates of ulcer complications with non-selective NSAIDs were similar in the two studies. There were no mortality differences for either COX-2 inhibitor versus COX-2 preferential NSAIDs or non-selective NSAIDs. Patient populations and study designs differed making comparisons between CLASS and VIGOR difficult.

The NSAIDs Subcommittee concluded by consensus that there is a statistically significant difference favoring rofecoxib in reducing the frequency of serious gastrointestinal events,
particularly gastrointestinal bleed, in comparison to a non-selective NSAID. For a composite endpoint of serious gastrointestinal events and symptomatic ulcers, celecoxib was found to be superior to ibuprofen and diclofenac in patients not treated with aspirin. The number-needed-to-treat to prevent a serious gastrointestinal event was comparable for both. There are still no studies evaluating the safety of valdecoxib in regards to serious gastrointestinal events.

b. COX-2 preferential NSAIDs versus non-selective NSAIDs

Evidence that meloxicam and nabumetone prevent ulcer complications compared to non-selective NSAIDs is weaker than that for COX-2 inhibitors. The main endpoint used in meta-analyses performed on trials of both of these agents was "PUB", perforation, symptomatic ulcer, or bleeding. There was a decrease in PUB’s in nabumetone compared to non-selective NSAID; no conclusions could be drawn about meloxicam. The meta-analyses were flawed because quality of the included studies was not assessed, and end-points were less well defined, raising questions about the validity of the conclusions drawn.

The NSAIDs subcommittee agrees by consensus that the evidence does not support the conclusion that COX-2 preferential NSAIDs are superior to non-selective NSAIDs in preventing ulcer complications.

c. Combination of a non-selective NSAID plus anti-ulcer medication

Misoprostol:

One good-to-fair-quality trial (MUCOSA) found that misoprostol prevented symptomatic ulcers and ulcer complications among patients taking non-selective NSAIDs compared to placebo. Misoprostol was associated with a high rate GI adverse effects, and led to a significantly higher rate of discontinuation of the drug than NSAID plus placebo.

The NSAIDs subcommittee agreed by consensus that misoprostol plus a nonselective NSAID is superior to placebo plus a nonselective NSAID in preventing symptomatic ulcers and ulcer complications, but with a high discontinuation rate due to diarrhea.
Proton pump inhibitors (PPIs) and H-2 receptor antagonists:

A Cochrane review summarized four trials of PPIs and seven trials of H-2 receptor antagonists. Strong evidence showed that PPIs and double-dose H-2 receptor antagonists reduce the risk of endoscopic gastric and duodenal ulcers. It could not be shown whether symptomatic ulcers or clinical ulcer complications are reduced. There are no head-to-head trials comparing PPIs and H-2 receptor antagonists.

No head-to-head comparisons of high-dose H2-receptor blockers to PPIs have been done. A trial comparing lansoprazole and misoprostol in patients who had a history of NSAID-induced ulcer showed higher withdrawals for misoprostol but equal efficacy on an intention-to-treat basis.

In one good study of patients with recent GI bleeding, there was no significant difference between celecoxib and diclofenac plus omeprazole; however, there was a high risk of recurrent GI bleeding in both groups.

The NSAIDs subcommittee agrees by consensus that:

- Although PPIs and H2-receptor antagonists with NSAIDs reduce endoscopic ulcers, insufficient evidence is available to conclude whether serious ulcer complications are reduced.
- Studies indicate that patients with recent gastrointestinal bleeding, whether on NSAIDs alone, NSAIDs with anti-ulcer regimen, or COX-2 inhibitors have a significant risk of recurrent GI bleeding.

3.2 Cardiac Events

One good quality trial (VIGOR) reported lower incidence of myocardial infarction in naproxen patients compared to rofecoxib. The rates correspond to a number-needed-to-harm (NNH) of one additional heart attack for every 333 patients treated with rofecoxib instead of naproxen. Serious thrombotic events (fatal and non-fatal MI, stroke, unstable angina, transient ischemic attack, resuscitated cardiac arrest, and sudden death) were higher in patients taking rofecoxib compared to naproxen, with a number-needed-to-harm of one additional serious thrombotic event for every 162 patients taking rofecoxib. A re-review grouped patients on whether treatment with aspirin was indicated based on cardiac prevention guidelines, i.e. patients at risk for cardiovascular disease. These patients treated with rofecoxib were five times as likely to have
an event. Patients not in this group were two times more likely to have an event.

One trial (CLASS) found that celecoxib had no statistically significant effect on the rate of cardiovascular events compared with diclofenac and ibuprofen overall and for the subgroup that did not use aspirin. Validity of these results is questionable; duration of the study may not be long enough to show an increased incidence of cardiovascular events.

The FDA has revised its labeling based on further reports from the CLASS study that found despite the twice higher than recommended dose of celecoxib, the rates of cardiovascular adverse events were no higher in celecoxib treated patients compare to ibuprofen or diclofenac treated patients.

By consensus, the NSAIDs subcommittee agreed that the evidence regarding risk of cardiovascular events with COX-2 inhibitors compared to the non-selective NSAIDS is inconclusive at present.

**e. Tolerability**

Trials show no difference between celecoxib versus non-selective NSAIDs and rofecoxib versus non-selective NSAIDs in withdrawals due to serious adverse events. GI adverse events, primarily abdominal pain, diarrhea, and nausea, were consistently lower for COX-2 inhibitors than for non-selective NSAIDs, even in studies that permitted the use of H-2 blockers in the NSAID group. In most studies these adverse events were described as mild or moderate and did not result in discontinuation of the drug. The magnitude of difference is probably one GI adverse event for every 20 patients treated.

Meta-analysis of meloxicam studies mentioned earlier found lower rates of any gastrointestinal event, dyspepsia, and withdrawals due to GI events compared with non-selective NSAIDs. It included inadequately blinded studies making it difficult to draw any conclusions. In the nabumetone meta-analysis, the incidence of GI adverse events was significantly different from the non-selective NSAIDs studied, corresponding to about one fewer event for every 34 patients treated with nabumetone.

**f. Renal toxicity**

The renal and hypertensive effects of COX-2 inhibitors and non-selective NSAIDs are not shown to be different. Two head-to-head trials found higher rates of renal complications with rofecoxib than with celecoxib. This difference may have been a dose effect.
g. Liver toxicity
Liver function data was insufficient to draw any conclusions about liver toxicity.

4. Are there subgroups of patients based on demographics, other medications, or co-morbidities for which one medication is more effective or associated with fewer adverse effects?

In most of the published trials, a majority of subjects were women. No publications focusing on the differential efficacy or safety of COX-2 inhibitors in African Americans, Hispanics, or other ethnic minorities were found.

A risk analysis in the United Kingdom revealed that serious GI complications from NSAIDs increased with age from 1:2100 under age 45 to 1:110 over age 75.

The NSAIDs Subcommittee agrees by consensus:
- The evidence does not support a difference amongst COX-2 inhibitors, COX-2 preferential NSAIDs and non-selective NSAIDs for efficacy or safety with respect to age, gender, race or ethnicity.
- They raised concern that for patients taking aspirin the benefit of celecoxib in reducing serious gastrointestinal events was obviated.
- In patients with recent GI bleeding all COX-2 inhibitors, COX-2 preferential NSAIDs, and non-selective NSAIDs should be used with caution because of the high risk of recurrent bleeding.
- In patients with hypertension there is risk of further elevation of blood pressure with all COX-2 inhibitors, COX-2 preferential NSAIDs and non-selective NSAIDs.

**Conclusion**

In a series of public meetings with the opportunity for public questions, comment and testimony, the NSAIDs Update Committee and Subcommittee of the Health Resources Commission reviewed the medical evidence comparing COX-2 inhibitors, COX-2 preferential and non-selective NSAIDs. All available sources of information including OHSU’s Evidence-based Practice Center report, Drug
Class Review on Non-steroidal Anti-Inflammatory Drugs (NSAIDs), and additional information presented in public testimony were considered.

Using all of these sources of information, the subcommittee and update committee arrived at the following conclusions about the comparative effectiveness and safety of non-steroidal anti-inflammatory drugs as supported by analysis of the medical literature:

**The NSAID Subcommittee found by consensus that:**

- There is no evidence to demonstrate a significant difference in efficacy among COX-2 inhibitors, COX-2 preferential NSAIDs and non-selective NSAIDs.
- There is raised concern that for patients taking aspirin the benefit of celecoxib in preventing serious gastrointestinal events was obviated. Even though evidence may demonstrate decreased adverse gastrointestinal events of COX-2 inhibitors compared to other non-steroidal anti-inflammatory agents, limitations of studies currently available for review preclude a confident conclusion overall that these are clinically significant safety advantages.
- Caution should be used in treating patients with recent GI bleeding with COX-2 inhibitors, COX-2 preferential NSAIDs and non-selective NSAIDs because of the high risk for re-bleeding.
- There are concerns about cardiac adverse events of COX-2 inhibitors, but data is inconclusive at the present time to draw definitive conclusions.
Frank Baumeister, Jr., MD  
Chair, Health Resources Commission

Diane Lovell  
Vice Chair, Health Resources Commission

Bruce Goldberg, MD  
Administrator  
Office for Health Policy & Research

Judy Zerzan, MD  
Chair, NSAIDs Update Committee

Kathleen Weaver, MD  
Director, Health Resources Commission

Health Resources Commission  
Frank Baumeister, Jr., MD  
Diane Lovell  
Steven DeLashmutt, MD  
Elaine Dunda  
Brad Bowman, MD  
Joanna Zamora, RN  
Paul R. Tiffany  
Walter Shaffer, MD  
Dean Haxby, PharmD  
Dan Kennedy, RPh

Non-steroidal Anti-inflammatory Drugs Subcommittee Members  
Ben Johnson PA-C  
Gerald Schoepflin, MD  
Jessie Ketcham-Zimmerman, PhD  
Joseph Schnaebel, PharmD  
John Tracy, PhD.  
Judy Zerzan, MD  
Paul Gorman, MD  
Stephen Acosta, MD  
Stephen Campbell, MD  
Donna Coy  
Michele Koder, PharmD  
Jim Norris, MD

NSAIDs Update Committee  
Judy Zerzan, MD, Chair  
Stephen Campbell, MD  
Walter Shaffer, MD  
Kathy Ketchum, RPh, MPA:HA  
Mark Helfand, MD  
Kathleen Weaver, MD
Health Resources Commission

The State of Oregon’s Health Resources Commission is a volunteer Commission appointed by the Governor. The Health Resources Commission provides a public forum for discussion and development of consensus regarding significant emerging issues related to medical technology. Created by statute in 1991, it consists of four physicians experienced in health research and the evaluation of medical technologies and clinical outcomes; one representative of hospitals; one insurance industry representative; one business representative; one representative of labor organizations; one consumer representative; two pharmacists. All Health Resources Commissioners are selected with conflict of interest guidelines in mind. Any minor conflict of interest is disclosed.

The Commission is charged with conducting medical assessment of selected technologies, including prescription drugs. The Commission may use advisory committees or subcommittees, the members to be appointed by the chairperson of the Commission subject to approval by a majority of the Commission. The appointees have the appropriate expertise to develop a medical technology assessment. Subcommittee meetings and deliberations are public, where public testimony is encouraged. Subcommittee recommendations are presented to the Health Resources Commission in a public forum. The Commission gives strong consideration to the recommendations of the advisory subcommittee meetings and public testimony in developing its final reports.