

# Health Resources Commission Meeting Minutes

DRAFT

February 20, 2004

**Members Present:** Chair, Frank Baumeister, Jr., MD; Diane Lovell; Walter Shaffer, MD; Brad Bowman, MD; Paul Tiffany; Dan Kennedy, R.Ph., James H. MacKay, MD

**Members Absent:** Mark S. Yerby, MD; Steve DeLashmutt, MD; Elaine Dunda; Dean Haxby, PharmD

**Staff Present:** Bruce Goldberg, MD, OHPR Administrator; Kathy Weaver, MD, HRC Director; Carol Anderson, HRC Assistant

## Discussion

### Roll Call and Approval of Minutes:

Meeting was called to order, by Chair, Frank Baumeister, Jr., MD, at 1:35 p.m. Roll call was taken. The minutes were approved as written.

### New and Departing Commission members:

Dr. Baumeister welcomes our new commission member, James H. MacKay, MD and asked him to tell a little about himself. Dr. MacKay stated that since the year 2000 he has been the Medical Director for Providence Health Plans of Portland. For the past 13 years he has been Chairman of the Pharmacy Committee and the Medical Director for the Providence Health Plan, he is on the clinical review committee and Chairs the Technology Assessment Committee for Providence Health Plan, and also he is Chair of the Utilization Review Committee. He comes to us with a great deal of knowledge about not only pharmaceutical but also new medical advances and was welcomed by the whole group.

Dr. Baumeister read a letter to Joanna Zamora, RN into the record, which stated on February 19, 2004. Dear Joanna, it is with regret that your tenure on the Health Resources Commission has expired. I have enjoyed serving with you while our charge was to encourage rational allocation of medical technology by informing health care decision makers about the cost effectiveness of medical technology and its impact on the health of Oregonians. Your contribution as a Commission member and expertise on health care advances for the last twelve years has been invaluable. Your professional and diplomatic demeanor contributed greatly to the successful implementation of Senate Bill 819 and the Oregon Practitioner-Managed Prescription Drug Plan.

I thank you on behalf of all Commissioners who wished that you had been able to attend the February 20<sup>th</sup> meeting for your farewell. However, we wish you the best and look forward to working with you again. Sincerely, Frank Baumeister, Jr., MD, Chair, Health Resources Commission. Copies of the letter were placed in the packets for each Commissioner.

### OMAP Update:

Testimony from Allison Knight, Policy Manager OMAP.

Allison Knight, Policy Unit Manager from OMAP testified that the rejection of Ballot Measure 30 has resulted in a number of cuts that need to be done to the Oregon Health Plan. The governors' priorities for keeping the OHP plus benefit package in tact and to continue coverage for children and pregnant women to 185% of the federal poverty level is to be enacted as best as possible. Noted in the governors' address however, OHP's standard will likely be suspended.

Allison Knight then went on to describe the OMAP PMPDP Plan Drug List Update; as of March 1<sup>st</sup> 2004 the Calcium Channel Blocker Class will be added with Norvasc and Lodipine (as a benchmark

drug), Nicardipine (generic), Nifedipine (generic) and Sular will be included in the preferred drug list. Also, the Statins will be updated to show that Lovastatin continues as the benchmark drug, but added to the list of preferred drugs are Altacor, Lescol, Lescol XL, Lipitor and Zocor. As of May 1<sup>st</sup> 2004 in the ACE Inhibitors Class will be added with Enalapril as the benchmark drug, but will include the following preferred drugs: Aceon, Captopril, Captopril HCTZ, Lisonopril, Lotensin, Monopril, Monopril HCTZ and Uniretic.

Next month Kathy Ketchum and Dean Haxby from the OSU College of Pharmacy will present on the OMAP educational efforts that will be focused on providers.

#### **Update on drug class reviews:**

Dr. Kathleen Weaver gave an update on drug class reviews. Estrogens, Oral Hypoglycemics and Skeletal Muscle Relaxants will be presented in their update reports today. Triptans have a full EPC Report that was received February 9<sup>th</sup> and the committee is being scheduled. Urinary Incontinence, the final update report was received February 3<sup>rd</sup> and a meeting is scheduled for March 10<sup>th</sup> for the Urinary Incontinence Update Committee. PPI had their first meeting on February 17<sup>th</sup> and are awaiting the final EPC Update Report. The Opioid Subcommittee has had their first and final meeting on February 17<sup>th</sup> and they will be presenting a report to the next HRC meeting. Statins and Nsaids reports are due the end of this month. Calcium Channel Blockers and ACE Inhibitors are due the end of March. The BB Subcommittee has its 5<sup>th</sup> and final meeting on March 11<sup>th</sup> and we anticipate that their report will be ready for the next HRC meeting on March 19<sup>th</sup>. The ARB preliminary report is due in April and the Inhaled Corticoid Steroid is not due until this fall. The updates are becoming like the twelve signs of the Zodiac and perhaps we will rename them with Pisces, Aquarius and Sagittarius by next meeting.

#### **Report from Oral Hypoglycemic Update Committee:**

Carol Blenning, MD, gave a report from the **Oral Hypoglycemics Committee Update**. She stated that in January of 2003 the HRC appointed an Update Committee to perform an evidence-based review of the April 2003 Oral Hypoglycemic Subcommittee Report for new information or changes in the Federal Drug Administration (FDA) package inserts. Members of the Update Committee consisted of one HRC member, one Oregon State University (OSU) College of Pharmacy pharmacist, one OHPR physician, one OHSU-EPC physician, and two Oral Hypoglycemic Subcommittee members. This report is an update of the initial April 2003 Oral Hypoglycemic Subcommittee Report.

The OHSU EPC's report, "Preliminary Update Report #1 on Oral Hypoglycemics" was completed in November, 2003, circulated to the Update Committee members and posted on the OHPR website at [www.ohpr.state.or.us](http://www.ohpr.state.or.us). The Update Committee determined there was not significant new information to recommend convening the original Oral Hypoglycemic Subcommittee. The Oral Hypoglycemic Update Committee met on December 15, 2003 to review the new evidence.

In the report new areas are highlighted for the audience's convenience. New findings of the OH Update Committee were:

- 1) The EPC received three dossiers from Pharmaceutical Manufacturer's and this information was added to the material and identified by the EPC in its search.
- 2) The OSU College of Pharmacy reported there was no new OH marketed in the US since April of 2003. There was however in September 23<sup>rd</sup> of 2003 an update to the Glipizide extended release in that there is an adverse reaction section of the product label included post-marketing abdominal pain.
- 3) Also, there was an update on Repaglinide to include gemfibrozil and itraconazole in the list of drugs that have been co-administered with repaglinide that result in longer half-lives for repaglinide.

4) The EPC using the same search strategy from the original OH report found 238 citations, but only 5 trials met the eligibility criteria.

5) One head to head trial found no difference in the effects of repaglinide and glimepiride on glycemic control after one year.

6) Clinically relevant outcomes repaglinide significantly improved treatment satisfaction, yet had no effect on well being or health status after 16 weeks in a placebo controlled trial of pharmacotherapy-naïve patients with type II diabetes.

7) Under subgroups a 2003 placebo controlled trial in Mexican American patients with type II diabetes showed that Glimepiride did not cause significant adverse events in this population. A open trial of 2003 of Repaglinide found that the rates of glycemic control, hypoglycemia, serious adverse events and deaths were similar for groups of type II diabetic patients with normal, mild to moderately impaired renal functioning, and those with severe or extreme renal impairment.

Moving on to the amended summary results on page 8.

**Key question 1**, for adult patients with Type 2 diabetes, do oral hypoglycemics differ in the ability to reduce HbA1C levels? The new additions to the text are that there are now eight randomized fair-to-good quality trials, but there was no clinically significant difference between them. Thus, the boxed consensus opinion has not changed.

**Key question 2**, for adult patients with Type 2 diabetes, do oral hypoglycemics differ in the progression or occurrence of clinically relevant outcomes? There was no change either to the text or to the consensus opinion in the black box.

**Key question 3**, for adult patients with Type 2 diabetes, do oral hypoglycemics differ in safety or adverse effects? Again, there was no change.

**Key question 4**, are there subgroups of patients based on demographics, concomitant medications, comorbidities such as obesity, or history of hypoglycemic episodes for which one oral hypoglycemic is associated with fewer adverse effects? There were no changes.

**In conclusion** it was the decision of the OH Update Committee that:

1) There is no clinically significant difference between any of the agents in these drug classes (oral sulfonylureas and non-sulfonylurea secretagogues) in their ability to lower HbA1c.

2) There is no statistically significant difference between glyburide and chlorpropamide in the progression or occurrence of clinically relevant outcomes with the exception of retinopathy. Patients on glyburide had greater risk reduction of progression of retinopathy than those on chlorpropamide. There is insufficient evidence on other sulfonylureas and non-sulfonylureas secretagogues to identify a difference in progression or occurrence of clinically relevant outcomes.

3) Chlorpropamide has a less favorable adverse effect profile compared to glyburide. There is no difference in safety or adverse effect profiles for other oral sulfonylureas and non-sulfonylureas secretagogues. Glimepiride, glipizide, glyburide, micronized glyburide and repaglinide do not differ in safety or adverse effect profile. No evidence exists for evaluation of tolbutamide, tolazamide or neteglinide.

4) There is no evidence that any one oral hypoglycemic is more effective or associated with fewer adverse effects than any other oral hypoglycemic agent amongst demographic subgroups including obesity.

5) There is no evidence comparing effectiveness and adverse side effects in the subgroups with concomitant medications, other co-morbidities besides obesity, or with a history of hypoglycemic episodes.

Are there any questions?

Chair Frank Baumeister, Jr., MD asked about the new finding from the EPC in which repaglinide significantly improved treatment satisfaction and yet had no effect on well being or health status after sixteen weeks and asked for more information on that.

Dr. Blenning was unable to answer that and Dr. Weaver asked Kim Peterson from the EPC. She said that it was only in treatment satisfaction, but on the more specific markers of well being or health status there was no change.

#### **Report from Estrogen Update Committee:**

Dr. Baumeister then asked Dr. Blenning to report on the Estrogen committee report. Dr. Blenning replied, HRC appointed an update committee to perform an EPC review of the June 2002 “**Estrogen For Treatment of Menopausal Symptoms and Prevention of Low Bone Density and Fractures 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 OHPR physician, one OHSU-EPC pharmacist, and two physicians from the original Estrogen Subcommittee members. The committee held one meeting held in public with appropriate notice provided.

The OHSU-EPC’s updated report “Drug Class Review on Estrogen For Treatment of Menopausal Symptoms and Prevention of Low Bone Density & Fractures Update Final Report #1 was completed in November 2003, and circulated to the Estrogen Update Subcommittee members and posted on the OHPR website at [www.ohpr.state.or.us](http://www.ohpr.state.or.us). The Update Committee held one meeting 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, and written and oral testimony. All available sources of information from the EPC’s report that included information submitted by the pharmaceutical manufacturers and public testimony, were considered.

Dr. Blenning then had the commission turn to page 8 where it has “**New Findings of Estrogen Update Committee, December, 2003**”.

1) Stated, the EPC received dossiers from three pharmaceutical manufacturers. This information was added to the material identified in their update search.

2) The OSU College of Pharmacy reported that there was a new transdermal vaginal ring (Femring, E2 50 mcg or 100 mcg) approved by the FDA in March 2003 for the treatment of moderate to severe vasomotor symptoms.

3) Using the same search strategy from the original OH report, the EPC found 123 citations, including 11 from the Cochrane Central Register of Controlled Trials, 9 from Medline, 60 from Embase, and 3 from pharmaceutical manufacturers. Ninety-nine of these were excluded at the abstract stage. Of the remaining 24 citations, 14 met inclusion criteria. Ten were excluded after full text review because of either the drug was not included, the intervention used combined drug therapy, or the study compared only different dosages of the same medication.

4) Two additional citations from the Women’s Health Initiative were published after the initial searches.

**Key Question 1.** What is the comparative efficacy of different estrogen preparations? Hot Flashes. Said on page 10, the consensus opinion was changed slightly to say the Estrogen Update Committee agrees by consensus that estrogen preparations improve symptoms of hot flashes/flushes. Head-to-head

clinical trials and placebo-controlled trials do not identify a clinically significant difference in estrogen preparations for the treatment of hot flashes/flushes. The other subgroups are sleep disturbances/night sweats, mood changes, urogenital symptoms/sexual function, quality of life were unchanged.

She then referred the Commission to page 12, Sub-Question 1B which is for preventing low bone density and fractures. There are now 52 trials meeting criteria comparing an estrogen preparation to placebo. The new information is that all but three trials combined and estrogen with progestins/progesterone therapy. In one small 135 patient trial conjugated estrogen increased bone density over three years at the femoral neck, total femur, and trochanter, but not at the lumbar spine. On page 13, although a minimally effective dose of estrogen to prevent bone density loss remains yet to be established. Middle of page 13, effect on bone density of discontinuation of estrogen was reported in two new independent studies and a follow-up study that concluded; the rate of bone loss after stopping estrogen was similar to that of women who did not receive estrogen treatment; after an average of 4 years (from the PEPI trial) there was no evidence of accelerated bone loss.

The consensus on bone density was only changed in the last sentence where it says; it is unclear if lower doses of estrogen **will** sufficiently preserve bone density. Will being the new word that was added.

Under fractures there was no change in the consensus opinion, so in conclusion there was no overall change in the key question 1 consensus, which reads. The Estrogen Update Subcommittee agrees that; estrogen preparations were found to reduce hot flashes/flushes, sleep disturbances/night sweats, mood changes, and urogenital symptoms. Studies measuring sexual dysfunction and quality of life were inadequate to determine any clinical relevance. No significant differences between types of estrogens could be determined. All estrogen preparations improve bone density; some studies demonstrate a dose-response effect. Use of estrogen reduces fractures. In both cases, no significant differences between estrogen preparations could be determined.

**Key question 2**, page 15, 2B sub-group breast cancer. A large cohort study of French women comparing users and non-users of estrogen over 8.9 years showed that the relative risk of breast cancer was 0.98 (95% CI 0.73-1.75) compared to non-users. Therefore the consensus statement under key question 2 has not changed.

**Key question 3.** Are there subgroups of patients for which one medication or preparation is more effective or associated with fewer side effects? Under the elderly, no studies specifically with elderly women were identified. Studies such as HERS and WHI and some osteoporosis and fracture trials enrolled older women (mean age mid-sixties). HERS/HERS II did not report results by age so it is currently not possible to know if older women had different benefits and harms than younger women from these studies. In WHI there was no evidence that the effect of CEE in reducing fracture risk differed by age or time since menopause. Also under the elderly, most studies have been done in Caucasian women in North America and Western Europe. The WHI reported a sub-analysis by race. Among black women (N=1124), CEE plus medroxyprogesterone acetate reduced the risk of fractures by 42%; however, this was not statistically significant because of the small number of fractures in this subgroup. There was no change in the final consensus on 3.

**In conclusion** it is the decision of the Estrogen Therapy Update Subcommittee that:

1. Estrogens reduce some menopausal symptoms and have been shown to improve bone density and reduce fracture risk. No studies showed any difference between estrogen preparations.
2. The majority of studies are of estradiol and conjugated equine estrogen (CEE). For many estrogen preparations, clinical trials are few and evidence is insufficient to conclude they are equal to estrogens that have been studied more extensively.
3. Evidence suggests that serious and nuisance side effects can be associated with hormone therapy. No studies compared the relative safety of different estrogen products.
4. At the present time there is no comparative evidence to evaluate estrogen use in subgroup populations of race, ethnicity or age.

5. The subcommittee feels that properly controlled comparative evidence is needed to better address these questions in the future.

Dr. Baumeister asked if there were any testimony or questions from the audience?

**Public Testimony on Estrogen Update Report:**

A member from the audience, Karen Murphy, FNP asked the question whether OMAP was covering combination Prempro as a preferred drug, even though it wasn't the benchmark drug. The reason she stated was she felt this was important because by taking the combination product women for sure get their progesterone and don't have the post-menopausal bleeding problems that lead to other diagnostic procedures which cost more money. Thus she recommended that the combination product be on the preferred drug list.

**Update Committee Roster:**

At this point Dr. Baumeister referred to item 12 on the agenda, which is the process updates. Dr. Weaver referred them to the document entitled Update Committee Roster, in their packets, which is a one page two-sided document. On the backside it has under Estrogen Update, Ken Burry, MD OBGYN Estrogen Subcommittee as a new member. Then under Urinary Incontinence it has Hillary Hotelling, MD, Geriatric, and Providence. Dr. Weaver responded that these are new physicians added to the update committee who have sent in their CV's and conflict of interest documents, which she has reviewed and recommends them for appointments. Dr. Baumeister then asked for a vote and it was unanimously approved.

**Other business:**

Other business, Dr. Baumeister referred to item 13. Dr. Bruce Goldberg gave an update on the Center for Evidence-based Policy. Basically the center has been functioning since the first of January and has 10 entities including 8 states that are contracted with them to obtain reports from the EPC. He emphasized that Oregon continues to be under contract directly with the EPC but is working collaboratively as part of the Center process. He emphasized that business will continue as usual and will remain seamless to the Health Resources Commission and then asked if there were any questions.

At this point Wally Shaffer, MD asked if there wouldn't be a difference in the way the key questions were handled. Dr. Weaver replied the appropriate sub-committee has developed the key questions for all 13 classes of drugs. The only new key questions for which the Center and the other State will be involved in developing the key questions are the Inhaled Corticoid Steroids. For the update questions the sub-committee from the Center for EPC has made only minor revisions to the well-crafted questions by our own clinical sub-committee. Therefore, there will not be any substantial change in the process. Dr. Weaver pointed out that if anything there would be an improvement of the process because now you get experts from all over the country that may think of new material that should be added to the key questions.

**Report from Skeletal Muscle Relaxant Update Committee:**

At this point a phone call was received from Dr. Josh Boverman to Dr. Weaver saying that he was going to be late for this meeting and not be present until 3:30 p.m., Dr. Baumeister then requested Dr. Weaver to give the Skeletal Muscle Relaxants report.

Dr. Weaver reported the HRC appointed an update committee to perform an evidence-based review of the **June 2002 Skeletal Muscle Relaxant 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 Skeletal Muscle Relaxant Subcommittee members. The committee held one meeting in public with appropriate notice provided.

The OHSU EPC's draft report, Preliminary Update Drug Class Review on Skeletal Muscle Relaxants for Spasticity and Musculoskeletal Conditions was completed in January 2004, circulated to committee

members. The update committee held one meeting 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, and 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.

Dr. Weaver then referred the commission to page 7, which listed the **new findings of the SMR Update Committee**.

- 1) The EPC identified six placebo-controlled trials of patients with musculoskeletal conditions and one placebo-controlled trial of patients with spasticity.
- 2) Two fair quality placebo-controlled trials evaluated the efficacy of metaxalone in low back pain and one poor quality placebo-controlled trial unspecified skeletal muscle disorders.
- 3) One fair quality trial evaluated the efficacy of tizanidine in patients with chronic tension headaches. One fair quality trial evaluated cyclobenzaprine in patients with fibromyalgia. One trial evaluated the efficacy of methocarbamol in patients with nonspecific muscle pain and spasms. One trial that evaluated skeletal muscle relaxants in patients with spasticity was a poor quality trial of methocarbamol in children with cerebral palsy.
- 4) There was enough evidence from a study summarizing case reports to suggest an association of chlorzoxazone with hepatotoxicity. This study evaluated 23 cases reported to the FDA since 1970 in addition to the case observed by the authors in 1986. Eight cases (two fatal) were judged to be probably related to chlorzoxazone, while the rest were possibly or doubtfully related.
- 5) A recent systematic review evaluating the effectiveness of skeletal muscle relaxants and benzodiazepines for acute nonspecific low back pain does not appear to change the results of the original report.

Dr. Weaver then referred the Commission to page 9, where it says **Amended Summary of Results**. She pointed out that in **Key Question 1A**, what is the comparative efficacy of different muscle relaxants; for reducing symptoms and improving functional outcomes in patients with a chronic neurological condition associated with spasticity? The only change was to increase to 36 placebo-controlled trials.

For **Key Question 1B**, what is the comparative efficacy of different muscle relaxants for reducing symptoms and improving functional outcomes in patients with a chronic or acute musculoskeletal condition associated with muscle spasms? There were several changes in the text including midway through the paragraph that there were now 20 placebo controlled trials that cyclobenzaprine is more effective than placebo. Methacarbamol was not as robust, yet with each of these interventions there was a consistent trend favoring the active treatment compared to placebo. Metaxalone was shown to be effective in two of the three available placebo-controlled trials. This did slightly change the consensus on key question one, which reads the subcommittee agrees by consensus that the evidence does not support a difference between the comparative efficacies of baclofen, dantrolene, or tizanidine for spasticity associated with chronic neurological conditions.

The evidence does not support a difference between the comparative efficacies of any of the skeletal muscle relaxants for muscle spasm.

Nearly all the studies for musculoskeletal conditions were limited to short-term treatment and showed only a modest clinical effect. Cyclobenzaprine had the largest body of evidence to support its efficacy. Metaxalone was not shown to be effective.

**Key Question 2**, what are the comparative incidence and nature of adverse effects (including addiction and abuse) of different muscle relaxants? New information added was there appear to be very rare cases

of hepatotoxicity with two fatalities out of 23 reported cases associated with chlorzoxazone, but the rate of complications could not be calculated from the reviewed study because the denominator of how many people who took chlorzoxazone was not met.

One new fair quality randomized controlled trial found that cyclobenzaprine 5 mg po tid provided equivalent effectiveness to 10 mg po tid regimen yet was associated with fewer adverse events. This could guide optimum dose recommendations and similar information that would be useful for other skeletal muscle relaxants.

In spite of diligent efforts of the EPC and our sub-committee, no evidence of systematic reports of addiction or abuse from skeletal muscle relaxants were available, although anecdotal evidence would suggest such tendencies.

The consensus opinion now reads for question 2 was the subcommittee agrees by consensus that there is sufficient evidence to conclude that there are different nuisance side effect profiles associated with baclofen, dantrolene, or tizanidine. Dantrolene is associated with rare but fatal hepatotoxicity and tizanidine requires monitoring of the liver function tests as it may also pose a risk for hepatotoxicity.

The evidence does not support any conclusions about the comparative safety of any of the skeletal muscle relaxants in patients with musculoskeletal conditions. There appear to be very rare cases of hepatotoxicity with two fatalities potentially associated with chlorzoxazone, but the rate of complications could not be calculated from the reviewed

There was insufficient evidence of the comparative risk of abuse or addiction with skeletal muscle relaxants, but the subcommittee notes that only carisoprodol and its active metabolite, meprobamate, are Schedule IV controlled substances in Oregon, although Meprobamate is not a federally Schedule IV controlled substance.

**Key Question 3** about subpopulations has no new information and there was no change to the consensus.

**In conclusion** it is the decision of the Skeletal Muscle Relaxants Subcommittee that the evidence does not support any conclusions about the comparative effectiveness between baclofen, tizanidine, or dantrolene for spasticity. All are effective and equivalent to diazepam. Dantrolene is associated with rare serious dose-related hepatotoxicity.

The evidence does not support any conclusions for the comparative efficacy between skeletal muscle relaxants for musculoskeletal conditions. Cyclobenzaprine had the largest body of evidence to support its efficacy compared to placebo. Metaxalone was not more effective than placebo.

Chlorzoxazone is associated with rare serious dose-related hepatotoxicity. The subcommittee notes that only carisoprodol and its active metabolite, meprobamate, are Schedule IV controlled substances in Oregon.

The evidence does not support any conclusions about the comparative efficacy or adverse effects for different subpopulations of patients such as race, gender, or age.

Dr. Weaver asked if there was any questions, there being none and there was no testimony from the audience, Dr. Baumeister asked for a vote on these three reports and they were all accepted unanimously.

**Other Business:**

Finally, Dr. Baumeister asked if there was any other business. It was brought up by Dr. Wally Schaffer that, "it seems to me that the HRC is involved in a multi step process to lower Oregon's pharmaceutical expenditures and we are doing our step very well, but the next steps are not being pursued by the

Department of Human Services because of the legislative restriction.” I suppose the PDL list is being updated periodically, but that is about it.

OMAP is doing a significant amount of prior authorization, but these are the preexisting rules. The Department of Human Services has lost its mandate to enforce the preferred drug list. Educational efforts and consumer efforts by the ALMA AART are important parts of the overall effort, but they are no substitute for point of service feedback in altering physicians prescribing behavior. Basically I think the HRC members should be apprised of this situation.

Allison Knight responded that at the next meeting we would be going through educational efforts of the DHS. Dr. Weaver said that efforts are going on between the OMA and the pharmacy committee, which she chairs. In addition she reported on a conference call from AARP National and ARP State who want to do an educational project focused on providers. Dr. Brad Bowman suggested that perhaps there could be involvement of the commercial entities such as WellMed or similar adventures that could use this information for commercial patients when they consider buying pharmaceuticals. From the patient standpoint this could be the co-pay from the purchaser’s standpoint it would reduce there cost if there were equally efficacious medications that cost less. Dr. Weaver suggested that perhaps the strategic planning session could be scheduled. She will discuss this further with Dr. Baumeister. Dr. Baumeister replied that he felt this was a good idea. He was concerned that the HRC has done excellent work, but it is “Like a prophet in their own land,” and not recognized by the providers or purchasers for their great contributions. He said that at these meetings the only audiences that are there to testify are against the process and that there are very few cheerleaders in the audience. However, it was very interesting what is being done here in Oregon from outside the state and we are being used as a model process.

The meeting was adjourned at 3:30 p.m.

**These minutes are in compliance with ORS 192.650. Only text enclosed in quotation marks reports a speaker’s exact words. For complete contents, please refer to the audiotapes.**

**Document Log:**

- Document 1: 11/21/03 HRC Meeting Minutes
- Document 2: Oral Hypoglycemics Update #1, December, 2003
- Document 3: Estrogen Update #1, December, 2003
- Document 4: Skeletal Muscle Relaxants Update #1, January, 2004
- Document 5: Update Committee Roster, 2003-2004

**MINUTES  
HEALTH RESOURCES COMMISSION  
March 19, 2004**

**Members Present:** Chair, Frank Baumeister, Jr., MD; Vice-Chair, Diane Lovell; Walter Shaffer, MD; Paul Tiffany; James H. MacKay, MD; Steve DeLashmutt, MD; Dean Haxby, PharmD

**Members Absent:** Mark S. Yerby, MD; Dan Kennedy, R.Ph.; Elaine Dunda; Brad Bowman, MD

**Staff Present:** Bruce Goldberg, MD; OHP Administrator; Kathleen Weaver, MD, HRC Director; Betty Wilton, HRC Project Coordinator

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**1. Call to Order**

Meeting was called to order by Chair, Frank Baumeister, Jr., MD at 1:35 pm.

**2. Roll Call and Approval of Minutes**

Roll call was taken. The Minutes for February 20, 2004 were approved with all in favor.

**3. New Commission Member**

Mark S. Yerby, MD was not in attendance.

**4. OMAP Update**

Kathy Ketchum, R.Ph., OSU College of Pharmacy, gave a presentation of the Oregon Health Plan Drug List Educational Initiative designed to increase clinician awareness and acceptance of the OHP drug list. Kathy discussed the educational plan that the college is proposing involving surveying high volume prescribing clinicians regarding their knowledge and attitudes. A survey form will be sent out March 22, 2004 to high volume prescribers to assess their awareness and attitude toward the PDL. Two to three weeks later a general education message will be sent. This will include a comparison chart of the individual prescribers adherence rate to the PDL compared to the mean rate of other OHP providers. Also enclosed will be the OHP pocket drug guide. This is a tri-fold pocket guide with the plan drug list on one side and the drug class cost comparisons on the other side. This pocket guide would be regularly updated and can be downloaded from the OregonRx website.

Prescription change forms will be sent with an explanation of the process for using the change forms. A resurvey will be made to assess a change in knowledge and attitudes.

Example of how this will work: If a patient was prescribed a non-PDL drug, a Rx form would be created based upon the claim data and include all info required to be a Rx. The physician would then evaluate whether a change was feasible, sign and fax back to the college. The change would occur at the next regular fill.

In the Fall, OSU will evaluate this based upon prescribing patterns, i.e. market share trends, which drugs are being used in each of the classes and at per member per month cost trends. Results will be reported to the HRC in the Fall.

Dr. DeLashmutt suggested a cover letter with a full explanation to the prescribers. He also suggested web access so that prescribers access information regarding why this drug is better.

Dr. MacKay asked how many doctors this would go to? Kathy responded this will go to 300 to 400 prescribers.

Dr. Weaver inquired what the market share baseline is at this time? Kathy Ketchum will report those numbers at the next meeting.

*Handouts: PowerPoint presentation; general message sample, sample survey form and sample pocket guide.*

**Action: No action required on this topic. Kathy Ketchum will report the market share baseline at the next meeting.**

## **5. Reports from OPIOID Update Committee**

Dr. William Origer presented the OPIOID Update Committee report. Dr. Origer reviewed the new findings of the Update Committee, and reviewed the Consensus statements. He directed the Commission to the Conclusion that did not identify any drug(s) as being more efficacious as any other. Dr. Origer summarized the conclusion stating that there was insufficient evidence to determine a superior product.

Dean Haxby asked regarding long-acting oxycodone vs. placebo, was there any discussion regarding statistical vs. clinical significance? Dr. Origer stated that the committee didn't get to that level of detail.

Dr. Shaffer inquired about methadone related deaths. Dr. Origer discussed the lack of data to validate the perception of an increase in methadone related deaths in Oregon.

Dr. Weaver stated that the committee will continue to follow the changes with each update. Dr. MacKay applauded the report and discussed the problems surrounding how oxycontin was being used.

No public testimony was given.

*Handout: OPIOID Update Committee Report posted on [www.ohpr.state.or.us](http://www.ohpr.state.or.us)*

**Action: HRC approved the report by unanimous vote.**

## **6. Report from Urinary Incontinence Update Committee**

Dr. Weaver stated that Dr. Ghetti could not attend and she will give the report for her. Dr. Weaver gave an overview of the findings of the committee that are stated in the report. One new drug was added, oxybutinin TD. The previous conclusion was changed to add oxybutinin TD. No other changes were made to the previous conclusion.

No public testimony was given.

*Handout: Urinary Incontinence Update Report posted on [www.ohpr.state.or.us](http://www.ohpr.state.or.us)*

**Action: HRC approved the report by unanimous vote.**

## **7. Update on drug class reviews**

Dr. Weaver gave an update on the other classes of drugs. PPI will have its second meeting on April 5<sup>th</sup>. Triptan 1<sup>st</sup> update meeting is scheduled for March 22<sup>nd</sup>. The Statin and NSAID full EPC report will be coming within a couple weeks and can then convene those update committees. The Statin review will require convening the full subcommittee. The EPC Preliminary reports on ACE and CCB are due the end of this month. The EPC Preliminary report on ARBs is due in April.

Dr. DeLashmutt asked if the ARB Subcommittee will look at treatment for congestive heart failure and survivability? Dr. Weaver stated that will be a criteria for review. She also stated that this subcommittee has a cardiologist and nephrologist.

## 8. Process Update

Dr. Weaver stated that due to the changes taking place when the dossier process moved to the Center for Evidence-based Policy that it necessitated updating the process document. Dr. Weaver stated that the new information is highlighted. There was discussion about the changes in the key question process. Dr. Goldberg discussed the key question process as it works now with the Center. Dr. Goldberg also stated that the state gets the same work at a reduced price. Oregon will still maintain autonomy. What the state loses is perhaps the small chance that there is some disagreement around a key question. If there is we can still go outside of the process to get the information that Oregon wants. After considerable discussion, it was decided that Dr. Weaver will create a flow-chart of the new system and old system process changes for clarification to present at the next meeting.

Dr. Weaver asked the commission to consider the standing update committee proposal outlined on page 2 of the process document. Dr. Weaver suggested that the standing update committee be composed of 1 HRC member (6 month rotation), 1 OMAP pharmacist, the HRC Director, 1 EPC representative, 2 physicians from previous subcommittees, and 1 pharmacist. In addition, 1 or 2 specialists would be consulted as needed for each review. Dr. Weaver discussed the difference between the EPC's preliminary and final updated reports and that the final updated report contains graded evidence and is the report used for the update committees. Dr. Weaver stated that this update committee could meet on a set schedule about 3 weeks before the HRC meeting and review more than 1 report if possible. If there is significant information that could change the previous conclusion, the original subcommittee will be convened.

Dr. DeLashmutt asked for clarification of the 3 steps we are currently performing? Dr. Weaver explained that there is a different update committee for every drug class and some meetings are very short because there is no change to the previous report.

Diane Lovell asked if there had been any discussion with subcommittee members about a different committee making a decision on whether or not there is anything to review? Dr. Weaver stated that it is very difficult to reconvene or to get members to serve as they didn't know they were signing up for a lifetime.

Dr. DeLashmutt suggested adding another step when there is data that changes the previous report, but not the conclusions, that the data go by mail to the original subcommittee members for comment back to the standing update committee. Dr. Weaver concurred.

Dr. Baumeister asked how much of this process can be done electronically? Dr. Weaver stated that the decision had been made to conduct these reviews in a public setting adhering to public meeting laws.

Dr. Shaffer stated he thought the standing update committee seems more efficient than the current process.

Dr. Shaffer asked for clarification on the difference between the preliminary and update reports and when they are used. After considerable discussion it was decided that Dr. Weaver will create a document clarifying the different reports to be presented to the HRC at the next meeting.

***Action: Dr. Weaver will create a flow-chart of the new system and old system process changes for clarification.***

***Action:*** Dr. Weaver will produce a document outlining the different reports and how they are used or produced.

***Action:*** HRC approved the standing update committee. Diane Lovell voted to modify step 2 with the addition that the EPC updated full report be sent to the original subcommittee to offer comment to the update committee, which becomes part of the record.

## **9. Center for Evidence-based Policy**

Dr. John Santa, Assistant Director for Health Projects, OHSU Center for Evidence-based Policy gave a presentation on the Center and the role it plays. Dr. Santa described the Drug Effectiveness Review Project (DERP) and how it started, which was an outgrowth of what was started by the Health Resources Commission. Dr. Santa stated that this project is an information strategy and takes the next step in globalizing evidence. The main focus of the DERP is to do systematic drug class reviews focusing on comparative effectiveness to support a variety of activities, which will vary with each participating organization. The objective is to pursue 25 drug classes, 12 of which have been done by Oregon, Washington and Idaho. This project runs for 3 years and updates will be conducted every 6 months. The project is designed for an enormous amount of input into the project from participants, local decision-makers, and pharmaceutical companies. Dr. Santa emphasized that the Center provides the evidence but does not make decisions and does not include cost effectiveness and focuses strictly on comparative clinical effectiveness. It is an information project not a purchasing or pricing project. The Center contracts with an EPC for the evidence-based reviews. The participating organizations contract with the Center for those reviews and give input into which drugs will be reviewed, give input into the key questions and timeline for the reports. Dr. Santa discussed the one-day conference for pharmaceutical companies being held May 24<sup>th</sup> in Chicago.

Dr. DeLashmutt asked how public input would be handled, e.g. for mental health drugs that are not reviewed here in Oregon? Dr. Santa stated that the other participants all have local processes and most have some accountability to the public.

Dr. MacKay asked if the Center spends much time on how to educate physicians? Dr. Santa stated that the Center does not do that and that it is up to the local decision makers.

For more information see the handout and the Center website: [www.ohsu.edu/drugeffectiveness](http://www.ohsu.edu/drugeffectiveness).  
*Handout:* Presentation slides are posted on [www.ohpr.state.or.us](http://www.ohpr.state.or.us)

## **10. Report from Beta Blocker Subcommittee**

Dr. Louise Kremkau, Chair of the BB Subcommittee, presented the report. Dr. Kremkau gave a summary of the report and the conclusion statements. Three drugs for patients with mild-moderate CHF were recommended for the PDL. Two drugs for patients with severe CHF were recommended for the PDL. Three drugs for patients with recent MI were recommended for the PDL. All drugs reviewed were found effective in the treatment of hypertension, and no differences were found between these drugs for blood pressure control, survival, or quality of life. All drugs reviewed, except carteolol, reduced anginal attacks in specific studies. Five drugs reviewed were found to be effective in rate control for atrial fibrillation. The current evidence for treating migraines did not identify any difference between drugs in this group used for migraine treatment. No difference was found for four drugs identified for treatment of reducing esophageal variceal re-bleeding. There were no drugs found superior for safety or adverse events. No differences were found in subgroups based on demographics, use of other medications or co-morbidities.

Dr. DeLashmutt noted that there are numerous blanks on Table 2 for propranolol. Dr. Kremkau stated that a blank box in the table indicates that the subcommittee didn't feel there was enough evidence to put any statement. Dr. Weaver stated that the subcommittee struggled as to how to represent hypertension which is the first column because all of the drugs have an FDA indication for hypertension, but the FDA criteria are not as strict as the EPC's criteria and that is why there is a star, it would have been confusing to leave it off the table. The table makes it obvious how little good evidence there is.

Dr. MacKay pointed out how expensive it is to do these studies and so many get moved to the back burner to make room for more politically important issues and cardiovascular is not at the top of the list.

Dr. Kremkau stated that most of the subcommittee's time was spent on heart failure and whether to break out the severe CHF from the rest of CHF.

Dr. MacKay inquired as to metoprolol tartrate when its not effective in heart failure but it lowers mortality after MI? Dr. Kremkau replied that the mechanism for preventing mortality after MI was different than after CHF.

Dr. DeLashmutt commended the subcommittee on a great report on such a confusing topic and that the report was made as clear as possible. Dr. Kremkau stated that actually reviewing the evidence altered long held opinions.

**Public Testimony:**

Dr. Bryan Gallagher, Senior Regional Medical Scientist for GlaxoSmithKline, offered testimony on the BB report. Dr. Gallagher commended the subcommittee for its work and that GSK recently reviewed the literature because of a new indication post MI. Dr. Gallagher stated that he did give testimony at all 5 of the public meetings held by the BB Subcommittee and that he learned a lot and shared some of the literature that was discussed with my colleagues. Dr. Gallagher stated that he had tried to delineate the post MI conditions as well as the classification of heart failure that is listed on Table 2. He stated he was in agreement on how the subcommittee classified heart failure. Stated the external validity of the final conclusions should be in concert with what other organizations have reviewed in the literature and made statements about. Regarding conclusion 1, carvedilol was given an FDA label indication for mild to moderate heart failure "class 2 and class 3 New York Heart Assoc Heart Failure". Stated that originally carvedilol was actually contraindicated in class 4 heart failure. GSK had to develop another study to submit to the FDA to be able to include the worst patients with heart failure. That's what the Copernicus study is and is referred to in the HRC report as a study of mild to moderate heart failure on page 13, but it was our severe heart failure study. The US Carvedilol trials were mild to moderate. We had to do an additional study to be able to close the gap in the treatment algorithm for class 4 heart failure to include all patients. The contraindication was lifted when we eventually got our approval from the FDA about 2001 for mild to severe heart failure. There was no New York Heart Assoc class included in the FDA description. It was just mild to severe heart failure and when you look at what the FDA reviewed our data for Copernicus, our severe heart failure study, they tried to compare it to the 4 trials that were combined in the US Carvedilol trials and tried to make comparisons to what already had been reviewed by the FDA and they found difficulty when they looked at the annual mortality rate, and this is available on the FDA's website and the very lengthy 370 page report that the EPC provided as background has a table 4 which lists the annual mortality rates for the US carvedilol trials and there is a wide disparity. In fact a trial that was supposed to have mild to moderate patients had a placebo mortality rate of 33.8 while the severe US carvedilol trials

actually had a mortality rate on this table of 8.6, so there was discrepancy and the FDA had difficulty trying to compare studies based upon annualized mortality rate to say they are equivalent. That's actually in the description from the FDA when they reviewed our study for Copernicus. So, when the equivalency of the two products that are listed for severe heart failure as in the consensus statement conclusion here it is, one of the products is not based upon data that was supported by the FDA in your initial review for the indication. We are the only product that actually has the spectrum from mild to severe heart failure. Its not a New York Heart Assoc. class description but previously in our labeling we had a contraindication before it was changed and taken out and we were all-inclusive, using those terminologies, so there is differences because the other product has NY Heart Assoc class II and III. What about class IV, the severe patients? Why were they not given approval at the time of submission, and I think its important for people to realize what the FDA reviewed and their final conclusion about patient number because when the FDA approves a drug for an indication, it is not just efficacy, it is also safety, and where in this report if we are going to have a statement about both providing efficacy in severe heart failure, the other part of that is what about safety, because you might treat patients that come to the state of Oregon on carvedilol, qualify for the OHP, severe heart failure, if Coreg is not included as at least one of these drugs for severe heart failure, then it will be switched over, presumably it will be metropolol XL (succinate), that is the other drug that is listed. Where is the evidence of the safety in doing that, especially since the original review of the information did not include all of the classes of heart failure, so I think that is important. In a conclusion about efficacy is based upon, in the severe group, a post hoc subgroup analysis of the trial that supported the mild to moderate...in class II, class III indication and there were only 40 patients actively being treated. Carvedilol actually in a subset in the New England Journal article of the Copernicus study, had over 300 patients - the worst of the worst. These were EF's less than 15 percent decompensation, so we know not only is the point estimate on the side of favoring carvedilol, the confidence intervals actually were totally also in favor. So, it was definitive and then there also were tolerability and safety issues that led to the FDA indication. So, that's point #3.

I will finish up my comments with the post MI condition. You think about a patient in Oregon presenting in a rural area with a MI, hopefully they have the advantage of modern therapy as Dr. MacKay alluded to metropolol tartrate as well as propranolol LA that are listed here in statement #3 for recent MI the studies respectfully go back to 1981 and 1982. Well, a lot has happened healthcare since 20+ years ago. Hopefully, even in rural Oregon they have the advantage of thrombolytics. Maybe they don't get an intervention but the CAPRICORN study that came out that led to the FDA indication for post MI with Carvedilol last year about this time had a very specific delineation by the FDA. This was different than the other 2 drugs that have an FDA indication that are listed there. The other one that's not listed is Atenolol but it was only in the short term. That was the ISIS-I study, the first 7 days. The group has decided to look at the outpatient follow-up for MI. Coreg with the CAPRICORN study got an FDA indication based upon left ventricular dysfunction with or without symptoms, so an EF less than or equal to 40%. That's a unique subset of patients so when a statement is that at least one of these 3 drugs that are listed there must be included in the PDL, if Carvedilol is not included in the post-MI condition, what is the Oregon practitioner going to do for a post MI patient who unfortunately does not have the advantage or success of modern therapy, who suffers injury to their heart, damage to the myocardial resulting in left ventricular dysfunction with or without symptoms of heart failure? What do they do that is evidence-based and FDA approved? They will not have an option based upon drugs that have studies 20+ years ago in an era totally different than today. So, I think the way that some of the conclusions of at least one or more of the drugs as mentioned here, and I agree with the way the statement is made, is that you have to think of some of the scenarios, that practitioners themselves are going to be put in. What about post MI

with LVD plus or minus symptoms, that's a unique group of FDA indications. In fact, metropolol (tartrate) and propranolol still have warnings in their labeling about heart failure, so I think it is very important for the practitioners to have an option that is approved and rigorously been defined as a group to receive benefit and safety by the FDA and I don't think the final conclusions can contradict what that body of the report has done to advance the field to allow us to have therapy to treat these very difficult patients. Heart failure is a serious disorder and the mortality rate, (I said this at my last public testimony for the ADA in San Francisco) was higher than a lot of cancers untreated, event treated heart failure is higher. COPERNICUS had a mortality rate that is listed in the mortality rate listed in the placebo group of almost 21%. So, patients lives are at stake and at extremes of the vulnerable patient with post MI who has had pump dysfunction, these patients have a higher mortality rate than any other than severe. How can we sell them short and give them something that doesn't have the evidence that even the FDA has been able to grant for them as an approved indication for the product? Thank you.

**End of testimony by Bryan Gallagher, MD**

Dr. Kremkau stated the subcommittee dealt with these issues and thought a lot about heart failure and severe heart failure and felt that there is no doubt that the COPERNICUS study, which evaluated Carvedilol, identified a high risk subgroup of patients defined by ejection fraction and symptoms, although they were not categorized by the general NY Heart Assoc classification. They were patients with symptoms at rest or minimal activity. But according to the data provided to us by the EPC and a subgroup of the MERIT heart failure trial, which evaluated metropolol succinate, was able to find 800 similar patients who essentially had very similar numbers in terms of mortality, the NNT to treat for each, for carvedilol and metropolol (succinate), based upon that evaluation were the same, until they are studied head-to-head. There was a big trial, the COMET trial that received a lot of attention this past year, but that evaluated metropolol TR (tartrate) against carvedilol. The study was started before metropolol succinate ER or just as it was being released. So, again part of the difficulties we face now are these very expensive trials, long term mortality trials, for the many drugs that we have now. It is a controversial area.

Dr. Weaver stated that it points out that ideally you would compare apples to apples and have the metropolol succinate compared to the carvedilol, but that trial hasn't been done and I don't know if it will be done. So, we have to use the evidence that we have. Dr. Weaver asked Dr Kremkau how many patients she sees in severe heart failure as compared to mild heart failure?

Dr. Kremkau stated that cardiologists see a special subclass of those that continue to have problems, in my practice probably a lot fall under that definition. Dr. Kremkau stated that the whole field has not been studied and one tiny little study on atenolol was done in Europe that showed benefit but it was abandoned after these other 3 studies were considered. It was not mortality, it was mortality plus the end points of that study, atenolol study the mortality plus worsening heart failure and it was stopped after a year because atenolol patients were doing better and decided not to do more because the other 3 studies had been published and were much bigger trials with thousands of patients.

Dr. DeLashmutt asked staff that didn't it seem in the past that the HRC had not made recommendations about what ought to be on the PDL, but have just recited the facts?

Dean Haxby stated that he thought the way the Conclusion was stated was great.

Dr. Weaver stated that the subcommittee agonized over how to present this information. We could have just taken each consensus statement and repeated it in the conclusion, but it gets to

be pretty confusing. The subcommittee decided that this was a way to prioritize what they thought were the important take-away points, and so that's the way they did the conclusion. If there were cases where a drug was not effective, we didn't include it, but where there were comparators that were equally effective, then we wanted to make the point that at least one of those for that particular condition be included. It is more prescriptive, but we were trying to make a report that could be used. The way I look at it is, people read these reports backwards, they probably start with the conclusions, then they go to the table and notice there is not a lot of evidence and then if they want to find out about those specific things they can go back to the consensus points. If they really want to know more they can look at the body of the report, and if they are really into it, they can go back to the EPC report that's 140 pages. It is sort of a pyramid of information. Each subcommittee writes their report independently yet we have some sort of general format. I appreciate Dean's comment, maybe from the pharmacist standpoint, this makes more sense.

Dean Haxby stated that his personal bias is that is the point of having a subcommittee to get expert opinion into the recommendations. I have actually felt that previous reports have actually been just a summary statement of some of the evidence components without really coming forward with some recommendations the committee felt was appropriate. So, I think this makes it very easy and much more useful for anyone looking at the document.

Dr. MacKay stated that this is very different from the UI report where you say they are all the same because you have so many evidences that you have to look at and so many different things that these drugs are used for and you are going to have the same trouble with ARBs. When you do that you'll probably come up with the same kind of conclusion. I think they are excellent and really are helpful.

Dr. Shaffer stated that he approves the change as long as we are aware of it. The alternative would be to like in recommendation #1 to leave off the second sentence. It makes it clearer what the subcommittee wants to say by including the second sentence so I guess our process is to give advice to the DHS and OMAP. That's direct advice.

Dr. Kremkau stated that because the subcommittee was dealing with mortality and these were drugs in a specific disease entity where mortality could be affected, that we felt strongly, particularly for #1.

Paul Tiffany agreed that the report was great and recommended making future reports in this format.

No other public testimony.

**Action: HRC approved the BB report by unanimous vote.**

No further discussion.

**Meeting adjourned.**

Handouts:

2-20-04 HRC Minutes	BB Subcommittee Report
HRC Roster	PMPDP Process
OPIOID Update Report #2	Center for Evidence-based Policy slides
UI Update Report #1	

**MINUTES**  
**HEALTH RESOURCES COMMISSION**  
**April 16, 2004**

**Members Present:** Chair, Frank Baumeister, Jr., MD; Vice-Chair, Diane Lovell; Walter Shaffer, MD; Paul Tiffany; James H. MacKay, MD; Steve DeLashmutt, MD; Dean Haxby, PharmD; Mark S. Yerby, MD; Dan Kennedy, R.Ph.

**Members Absent:** None

**Staff Present:** Kathleen Weaver, MD, HRC Director; Betty Wilton, HRC Project Coordinator

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**1. Call to Order**

Meeting was called to order by Vice-Chair, Diane Lovell at 1:35 pm.

**2. Roll Call and Approval of Minutes**

Roll call was taken.

**Action:** *The Minutes for March 19, 2004 were approved with all members present in favor.*

**3. OMAP Update**

Allison Knight, Medical Assistance Program, gave a brief update. She indicated that OMAP did receive approval from the Centers for Medicare and Medicaid Services on the Managed Care Provider Tax and that tax will help them fund a portion of the Standard Benefit Package, which was scheduled to end in August. The number of people currently covered will be reduced.

Effective June 1<sup>st</sup>, there will be a few changes to the Plan Drug List. In the Estrogen category, the benchmark drug is Estradiol, others included are Cenestion, Menest, Ortho-Prefest, Premarin, Premphase, and Prempro. The other class being modified is the Oral Hypoglycemics. The benchmark drug is Glyburide and the other drugs included are Glipizide, Glyburide Micronized, and Tolbutamide.

Dan Kennedy commented that Ortho-Prefest is no longer called that but is now simply called Prefest.

**Action:** *No action required on this topic.*

**4. Process Update**

There was considerable discussion about the draft PMPDP Process document. Anne Tweedt, BristolMyersSquibb, expressed concern that the public would not have the opportunity for public comment on new or updated Key Questions, as they have in the past, before the Key Questions were presented to the HRC.

Dr. Weaver advised that the document would be revised to allow for the Key Questions on new drug class reviews to be presented in a public subcommittee meeting before they are presented to the HRC.

HRC members expressed concern that Anne Tweedt's requests were valid and that Staff is to return to the next HRC meeting with a revised proposal on how to give the public a more open opportunity to give input on the draft update Key Questions.

Dr. Weaver discussed the proposed members for the Standing Update Committee to be one HRC Director, one OSU pharmacist, one HRC member, one EPC member, two MDs and one pharmacist. They will look at the EPC update reports and if there is a minor change they will amend the current report. If there is new information that could change the Conclusions then the original subcommittee will be convened. Dr. Weaver asked star performers who have served on subcommittees and been previously approved. Dr. Jody Pettit and Dr. David Labby have agreed to serve. Nicole O'Kane, Pharmacist, or Jim Slater, Pharmacist, may also serve. Dr. Weaver asked for an HRC volunteer to serve for six months. Paul Tiffany volunteered.

*Handout: PMPDP Process*

***Action: HRC approved revising the process document to add the convening of the new subcommittee to review the KQ in a public meeting as in the past, and a process change to page 2 and the revisions will be presented at the next meeting. HRC approved staff moving forward with the process. All approved. Paul Tiffany volunteered to serve for six months on the new Standing Update Committee.***

## **5. Status of Drug Class Reviews**

Dr. Weaver stated that the NSAID and Statin EPC Updated Final Reports were received. Due to the major changes indicated in the Statin report, the original Statin subcommittee is being convened. The new Standing Update Committee will be convened to review the NSAID Updated Final Report. Dr. Weaver stated that ACE Inhibitor and Calcium Channel Blocker EPC reports would be received soon.

Dr. Weaver discussed the proposed PPI Update #3 draft Key Questions, which included language regarding treating patients stratified by severity of their esophagitis. She stated it makes the Key Questions more specific but doesn't really change it.

Dan Kennedy stated that at the end of the previous update meeting there was some discussion about whether there was a real difference in PPIs regarding treatment of severity of erosive esophagitis. The discussion was brought up in the update committee and there were individuals on the committee that were uncomfortable that it was not previously mentioned and the consensus was that the recommended change should be made to the EPC.

Dr. Weaver stated that there was public testimony on this topic at the update committee meeting.

Dr. Shaffer stated he assumed that the "stratified by severity of severe esophagitis" means by endoscopic severity? Dr. Shaffer suggests that it could read "severity by endoscopic criteria".

Kathy Ketchum stated that as a member of the update committee there were two different methods of severity grading that we used in the literature and perhaps more and suggested leaving this more open ended so the EPC can collect more evidence.

Dr. Baumeister stated that he didn't see a problem leaving that language as both methods utilize endoscopic.

No public testimony offered.

*Handout: PPI Update #3 Draft Key Questions with proposed revision*

**Action: HRC approved the revised Key Questions with the additional language of "severity by endoscopic criteria".**

## **6. Triptan Update Committee**

Nicole O'Kane, Pharmacist, gave an overview of the findings of the Triptan Update Committee, which is outlined in the Triptan Update Report #1. Nicole stated that the recommendations did not change from the previous report, even though there was a new drug and numerous studies to review. Nicole also discussed the implications of encapsulation and how it affected the studies. Dr. Weaver briefly discussed some of the highlighted changes.

Dr. Yerby stated that migraine is mainly a disease of women in the child-bearing ages, issues of relative safety in pregnancy would be important for practitioners to know about that data. Dr. Weaver asked the EPC if pregnancy was looked at as a separate category? Kim Peterson stated it would have been looked at under KQ#3 and would have reported it. Dr. Weaver stated that she would keep a lookout for that data on future updates.

Nicole discussed the importance of the committees not focusing on what they are not tasked to do and not making a guideline.

No public testimony offered.

*Handout: Triptan Update Report #1*

**Action: HRC unanimously approved the Triptan Update Report #1.**

## **7. Report from PPI Update Committee**

Dan Kennedy, R.Ph. gave an overview of the findings of the PPI Update Report #2. Dan stated that the Conclusions did not change from the previous report.

### Public Testimony

My name is Doug Levine. This is Bruce Bishop. I represent AstraZeneca, a manufacturer of Omeprazole magnesium. I am a physician and gastroenterologist and my role in the company is as Executive Director in Strategic Development and clinical research and what's known as the development brand leader for Nexium. So, want to make sure you understand I have a permeation of business accountability for Nexium but also a medical side accountability regarding efficacy and safety of the product as marketed in the US. The purpose of my testimony is ultimately to ask the HRC to consider not accepting the current version of the report

and I will explain why. In preparing for, in just the past few weeks, getting familiar with the HRC process, having the opportunity to review the full EPC report and the PPI Update Committee Report, there are two general areas of concern though that I would like to offer comments on. First is just the evidentiary process and issues related to scientific validity as it relates to the EPC report and the summation report as prepared by the update committee, and then specific evidence issues with regard to Esomeprazole.

Regarding the process points, I would just say personally I can appreciate the state's process for developing policy on health care expenditures and my presumption, my premise, in these comments is based on my understanding of the process where policy is derivative to scientific evidence, and certainly given what is at stake for the citizens of Oregon, I would think that you would agree that it is important, if not imperative, that the scientific foundation or the scientific pillar is very, very important for the determination of the policy. While we appreciate the intention of the scientific efforts of the EPC in generating its drug class review, particularly in the PPI group, I have to ask the HRC if they are confident that the EPC report on PPIs meets generally accepted scientific quality standards, before considering approving it, and I would like to suggest that all of these standards may not have been met by asking a few of my own, if you will, key questions.

First, "Should not the reports be based on scientific standards of strong, rigorous and complete review of evidence?" I would expect the answer to be "yes". But I would submit that limiting the review to clinical trial reports may not be appropriate. I think that a full understanding of the fuller meaning of the trial reports would be derived by the EPC having an opportunity to have more broad review capabilities that would look at topics such as pharmaceuticals or drug chemistry, basic pharmacology including pharmacokinetics, other references related to disease per se, in this case gastro esophageal reflux disease and other acid related diseases, and epidemiology and natural history of disease. I think another body of evidence that has not necessarily been documented to be included would have been the variety of US federal regulatory literature that pertains to the FDA drug review and approval process of drugs, and a lot of information is available through Freedom of Information Act, as well as the ability to formally review approved product labeling, and these deficiencies, I think, could affect the overall determinations or answers to the Key Questions put forward. I also just want to reference the other discussion on Key Questions that the potential danger in the Key Question process, and I recognize fully HRC's desire to have a very open public process, is that to some degree those questions can be constraining from the scientific view, in offering the broadest perspective to help answer the very broad questions that the Commission wants to get at.

The second question is, "Should not the evaluation of literature data be conducted by qualified experts in the field, thus reflecting the highest standards of expertise?" While I absolutely respect the expertise of the EPC in conducting the evidence reviews of clinical trials, I have to ask whether or not there were other individuals with specific expertise in gastro- esophageal reflux disease, basic science, clinical science, and clinical trials to help in that evaluation along with the evidence review specialists? I submit that certain perspectives regarding adequately broad interpretive power were missed by not inclusion of all these experts.

The third point, "Should not the reports lack bias to be consistent with scientific standards of objectivity?" Evidence-based reports, I think you would accept, should justify with evidence all statements. The PPI reports unfortunately contain interpretive statements without citing any evidence foundation and include assumptions without citing any evidence foundation for those statements. Lastly, were selective rather than inclusive in the review of published literature and

considerations of other information sources such as comments by the FDA. So, these statements fundamentally create the impression of bias.

Fourth question would be, "Should not the report be peer reviewed to allow for reconciliation of differing and valid scientific views." Although this is spoken to as part of the overall process within the state, there is no indication in the EPC report that a peer reviewed process was conducted.

Finally, "Should not the findings or conclusions of these reports be subjected to scientific standards involving the demonstration of reliability?" Again, the EPC report and PPI Update Committee Report, nor does the process, call for assessments of replicability, which is fundamental to the scientific process.

I would next like to move to areas of specific evidence concerns I had regarding the PPI report. At issue here are contents of the report that make claims assertions and interpretations that are either not projected ....or are not informed because of a failure to exam all relevant sources of information. As I alluded to before these deficiencies at least creates the perception of bias in the reports. So, for instance, what is the evidence for claiming "poor applicability of the dosage comparisons of Esomeprazole 40mg and Omeprazole 20mg? In other words, that somehow these data are not as valuable because there weren't data available to compare the 40 mg vs. 40 mg doses of both drugs. I would suggest that review of some of the other pharmacologic literature, if that had been allowed, would have allowed the EPC to not necessarily demean the available evidence that is there. Second point is what is the evidence proclaiming that the differences in healing of erosive esophagitis are "small" or "clinically irrelevant". I would submit that there was really inadequate examination within the reports to explain these differences such as looking at baseline severity of disease, or looking at disease epidemiology to understand the ramifications of these data differences, which would, in fact, provide potential benefits to many thousands of patients within the state.

I would ask, third, "Why has the evidence review by FDA apparently been ignored based upon not comparing the product labeling because if that were done one would find that Esomeprazole, in fact, is the only PPI that the FDA has allowed approved labeling that compared relative efficacy to another PPI; in this case Omeprazole. That's not the case with the other PPIs. I would ask, "Why certain literature was excluded because of lack of availability of crude healing rates when these data were easily derived from the information that was in that article.?" Next I would ask, "Why was there not better assessment of primary hypothesis testing and statistical power assumptions in different head-to-head clinical trials, given the fact that virtually all these trials are understandably subsidized by the pharmaceutical industry in a very competitive environment, and those study designs become important in understanding and interpreting the results of those studies." Lastly, I would simply ask, "Why have FDA approved doses for certain indications been ignored? In this case, there was some discussion about studies looking at the maintenance of healing erosive esophagitis where the study results were cast aside because they were not what are deemed to be the most common prescribed doses and the FDA approving specific doses is based on evidence evaluations suggesting the optimal dose is what the approved dose is?" So, it is something that I am surprised at.

So, in summary, based on what is at stake for the citizens of Oregon, I think that there are deficiencies in the EPC report and in part, these are based on both some process deficiencies that I have suggested as well as some deficiencies in the review of evidence. Some misinterpretations and incomplete assessments of easily available data have led to a conclusion that the PPI are equally efficacious when despite acknowledgment in the EPC reports that

statistically significant differences this has not really been carried forward to the final conclusions at least to the key question. So, I would make an appeal to the HRC not to accept these versions of the reports until the deficiencies can be corrected. I want to be very clear that I am not advocating for any sweeping superiority claim of my company's product in the PPI class, but I am advocating for correct scientific characterization of the evidence in their reports and their conclusions. While I recognize the challenges in instituting policies that have broad affects in the state's patients, I am asking that the HRC recognize the individual medical needs of different patients within the state because some will unequivocally realize benefits with treatment of esomeprazole that they would not necessarily with other PPIs. So, I am asking that the HRC not, by virtue of the process and the current status of the report, mislead patients and doctors about this subset of patients who will enjoy differential benefits with the product, but also ask HRC not to compromise the evidence that, in fact, favors esomeprazole and that has been recognized by some degree by the EPC in it's report, other managed care organizations and states, physicians, the FDA and other regulatory bodies around the world. I would ask that the HRC to insist on clearer separation in the reports of scientific evidence as opposed to determinations of policy based on evidence because any blurring of that distinction will be of no benefit in the long run. I will be happy to provide formal, will file my testimony in a formal fashion as well as past testimony that has been provided to the PPI Update Committee, as well as a Memorandum of Revisions of the April 2004 PPI Update Committee Report, which Bruce Bishop would like to address.

End of testimony for Dr. Levine

I am Bruce Bishop. I am the legislative advocate for Astra Zeneca. When we participated in the PPI Update process we did submit specific recommendations. Those were fashioned into an earlier version of the report and so we had modified those recommendations to reflect, I believe, the most current version of the PPI report. There were a few modifications, at least editorial changes, made since the update, but I think we have addressed the substantive issues and will be glad to offer these specific recommendations to identify ways in which we think that the PPI report can actually be conformed to the evidence found by the EPC. That's a piece of what Dr. Levine has addressed in terms of the overall concerns that we have. But we have tried to focus our recommendations specifically on the product that you are looking at, which is the translation of the EPC report into an update report that would be generally distributed....There are deficiencies in the way that translation has taken place and we have tried to correct it in these recommendations, which I will leave with the staff for your further consideration.

Dr. Weaver asked if these recommendations were different than those he handed out at the update committee meeting? Bruce responded that they are substantively the same, but was not compared to the most recent version.

Dr. Weaver stated that their testimony was in response to the EPC report and asked if AstraZeneca provided feedback to the EPC in their peer-review process, and if so, what was the response? Dr. Levine did not understand the peer-review process. Dr. Weaver stated that the EPC posts their reports and then asks for peer review. Dr. Weaver asked if they had responded directly to the EPC with their concerns? Dr. Levine stated that due to the time period he had been involved that he had not directly but only through the public testimony. Dr. Levine said he had accessed the website and viewed the February 2004 EPC updated final report and the HRC Subcommittee report.

Dr. Weaver stated in response to Dr. Levine's question regarding why the HRC doesn't rely on experts in this area, she stated that most experts do not meet the conflict of interest criteria required by a very public process. She stated that the EPC are experts in reviewing the

evidence and they rely on the clinicians, both pharmacists and physicians, in the subcommittees to look at the applicability of that particular evidence.

Dr. Baumeister stated, “that we don’t have any experts, that they are just country doctors here, but Judy Collins is a professor of Gastroenterology at OHSU. She is an acknowledged international specialist in inflammatory bowel disease and I am certainly sure she understands heartburn. Craig Fausel is a Gastroenterologist, in probably one of the largest Gastroenterology groups in Portland and been in practice about 25 years. I am a Gastroenterologist and I only started in ’64 so I think we have a few Gastroenterologists here too that have reviewed this. We made a decision long ago in this Health Resources Commission that we would deal with clinical issues that they were far and away the most important issues and I think that is where this comes from.”

Dr. Levine asked to respond. I respect that. First of all, I want you to understand that where I am coming from we are dealing actually with nuances regarding the final piece of the report just so that you are not thinking that I’m requesting sweeping changes. The second thing that I submit that I think you would respect is I fully trust the capabilities of the people that are involved and am asking for greater visibility to those with other expertise that could change the way clinical trial evidence gets looked at and I tie that specifically to a few comments that are made within the report where its clear that there had been assumptions made from a position where I suspect that people may not have had the expertise. The only way that I have to judge the report and whats in the report and you can glean subjective from objective statements, so that’s the first thing. The second thing is that there are a lot of other review bodies that allow for experts to be involved in the process even if there is a perceived issue of financial conflict. I think there that’s handled by full disclosure. So, granted I am raising questions about the process and would add that as another question why can’t other experts be involved even if, in fact, there is disclosure of potential conflicts, because what I fear on the other end is what is not protected is intellectual conflict of interest that may, in fact, be contributing to some of the disagreements here.

Dr. Baumeister stated that in the process, testimony is certainly not limited to people who do not have a conflict of interest. He stated that in the subcommittee hearings there is ample opportunity for testimony from anybody that is interested.

Dr. Levine: I understand that. My concern is that it’s the EPC report that is upstream from the subcommittee work and the HRC work and very much respect the open process that you allow public testimony but what you all are already dealing with is literally, “The horse is sort of out of the barn” with regard to what the EPC report is and I want to make clear that my concern of the process had more to do with what the EPC activities are and my sense is that they may be just a little hamstrung by either the nature of the questions, the type of literature that they allow to review and perhaps the other different expertise that could participate in the process within the EPC. That is the point I am trying to make.

Diane Lovell asked if the essence of his concern was that the EPC is constrained to reviewing reports that are public in nature?

Dr. Levine: Yes, there is a lot of published literature that wasn’t included or what seemed to be included was exclusively head to head clinical trials, and in fact, it was documents that not all of that type of literature, in fact, was reviewed, which in some cases may have been a mistake, but then there is other types of literature that deal with the pharmacology of the drugs that impact

some of the subjective statements that appear in the overall EPC report and that kind of literature appeared to not have been reviewed at all.

Diane Lovell stated that it is HRC that sets the standard of evidence that we want reviewed, and if there was any research that anyone felt was missed they have the opportunity to raise that at various times, so not sure why Dr. Levine feels constrained.

Dr. Levine: That literature was submitted in the dossier process. I am challenging, "That the subcommittee didn't choose to accept the recommendations) because I am concerned that the perception is that all the needs to be reviewed may be this segment of the literature and just from the scientific perspective I am suggesting to you based on my experience that that is potentially dangerous in that one may not have the full opportunity to have all of that availability in coming to a scientific conclusion.

Dean Haxby stated that he felt that they (EPC) were using the best levels of evidence to answer the questions that are being asked. Pharmacokinetic studies, pharmacodynamics studies are not the level of evidence needed to make this kind of comparison, and so its head-to-head clinical trials that really are the gold standard.

Dr. Levine: I believe the specific issue I have though is the diminishment of some of the head-to-head trials because of the dose selection, because of a presumption about what equivalent doses should have been. Whereas, if there had been and this may not apply to all drug classes but this specific class review, the omission of the review of the pharmacologic data essentially led to an unsubstantiated subjective comment and treatment of the data within the report.

Dr. Weaver asked for the EPC to comment.

Dr. Levine: May I just say that we met with Dr. Santa and I actually hoped because of the fact that I am 2500 miles away when I came out here hoping to have an opportunity to meet some of the EPC scientists. We were able to meet with Dr. Santa, who can't qualify, but we're trying to work on a way where appropriately in a transparent forum these sort of higher level issues that could impact the review of evidence might be able to be discussed, but we urge you to do the same please.

Susan Carson testimony:

I am Susan Carson, Research Associate for the EPC. I think the issue of the pharmacokinetics studies has already been addressed. Those studies were not part of our inclusion criteria and as has been mentioned clinical trials are the highest level of evidence and that is the evidence we used for the most part in the report. I think that the specific objection was to head-to-head trial of esomeprazole 40 mg vs omeprazole 20 mg and our point is that those doses, that omeprazole 40 mg would have been a more appropriate comparator to esomeprazole 40 mg and that comparison was not done in the study. There are four studies submitted to the FDA comparing esomeprazole to omeprazole. Two of those studies were published and are included in our report. Two other studies are in the FDA information but they have not been published and the reason we didn't include them in our report was not that they weren't published, but because they weren't reported in enough detail for us to assess their quality. So, I would like to point out also that the product label for esomeprazole does not state that the FDA concluded that esomeprazole is superior to omeprazole. Two studies had statistically significant results where esomeprazole was indeed better at healing rates at 4 and 8 weeks. The other two showed no difference between esomeprazole 20 mg and omeprazole 20 and esomeprazole 40 mg vs omeprazole 20 mg.

I would like to address the comments about peer review. There were gastroenterologists on the subcommittee who were involved in reviewing the report and we did send the report for peer review, the original report was peer-reviewed by several experts. Those comments and our responses are available from the EPC if anyone would like to see them. It was also reviewed by AHRQ (Agency for Healthcare Research and Quality). They made comments on our report and our report was revised based on those comments.

There was some objection to a couple specific statements in the report and one of the statements we did discuss at the update committee last week. The statement was that 3% difference in healing rates found in esomeprazole and omeprazole studies was not clinically significant. We didn't think it was a clinically significant difference. We talked about that and decided that that should indeed be taken out of the EPC report because it sounds like a judgment about whether its clinically meaningful and its not really the job of the evidence report. Our point was really and we did make that clear, that the 3% difference was similar to differences in other studies that weren't statistically significant, so that is what we meant when we said it was a 'small difference'. Whether that gets taken out of the subcommittee report is really a decision to be made by this commission because it is a decision about evaluating the evidence and interpreting the evidence.

There was a comment about crude healing rates in a study of omeprazole vs. esomeprazole, we criticized the study based on it's method of analysis that used the life table analysis to report healing rates rather than crude healing rates and I think that the comment was that this information was available in the report but I would like to point out that it wasn't and we have been looking for it and we've been trying to get it for some time including contacting the manufacturer to ask for that data. Also, we're not saying that the method analysis is inappropriate or wrong or an inferior method of analysis, but rather that it was different from the other studies so there was no way that we could directly compare the results in that study to the other results. We have spoken to our statisticians at the EPC and we have emailed and been in contact with the manufacturer to try to clarify this but we have not gotten a satisfactory response.

Paul Tiffany asked if the process the EPC followed in this particular case is the same it follows in every other case it does. Susan stated that was correct.

#### End of Public Testimony

*Handouts: PPI Update Report #2*

**Action: HRC approved the report by unanimous vote.**

## **10. Other Business**

Dr. Weaver gave a brief report on the Center for Evidence-based Policy Governance meeting that was held earlier this same week. There are now 12 participating organizations. There are 8 other organizations in the process of signing. The POs currently are primarily Medicaid state departments.

Dr. Weaver stated that Dr. Bowman moved out of state and therefore cannot serve on HRC. Dr. Weaver stated that Dr. Bowman represented “business” and he would be replaced and asked for recommendations for a replacement.

Dr. Weaver welcomed Dr. Yerby, who joined the meeting for the first time.

No further testimony.

**Meeting adjourned.**

Handouts:

3-19-04 HRC Minutes

PMPDP Process

PPI Update #3 Draft Key Questions

Triptan Update Report #1

PPI Update Report #2

**MINUTES**  
**HEALTH RESOURCES COMMISSION**  
**July 16, 2004**

**Members Present:** Chair, Frank Baumeister, Jr., MD; Vice-Chair, Diane Lovell; Walter Shaffer, MD; Paul Tiffany; James H. MacKay, MD; Steve DeLashmutt, MD; Dan Kennedy, RPh.; Elaine Dunda

**Members Absent:** Mark Yerby, MD; Dean Haxby, PharmD

**Staff Present:** Kathleen Weaver, MD, HRC Director; Carol Andersen, HRC Assistant

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**1. Call to Order**

Meeting was called to order by Chair, Dr. Frank Baumeister at 1:35 pm.

**2. Roll Call and Approval of Minutes**

[A-001]

**Action:** *The Minutes for April 16, 2004 were approved with all members present in favor.*

**3. OMAP Update**

Allison Knight, Assistant Manager for Program and Policy Section of OMAP, gave a brief update.

[A-020] Allison asked for support in adding the review of three more drug classes. She stated them as Anti-Platelet (AP), Alzheimers (ALZ) and Non-sedating Anti-Histamines (NSAH). Allison explained that the NSAH has been reviewed by the DERP and recommended that the HRC review it during the next update. Dan Kennedy asked if NSAH are not a covered item. Allison stated that OMAP would be looking at it for co-morbid conditions. Dr. Baumeister asked if a decision needed to be made. Dr. Weaver stated that no decision was needed at this time and talked briefly about other drug class reviews that are going to be done by the DERP that Oregon will not be doing. Paul Tiffany asked if Alzheimers fit into the mental health category. Dr. Weaver stated it was considered physical health. Kathy Ketchum confirmed that they are not part of the mental health carve out.

[A-073] Allison stated that Beta Blockers class has been added to the Plan Drug List as of August 1st, and the drugs on there are Toprol XL, Atenolol, Bisoprolol, Inderpan XL, Labetalol, Metoprolol Tartrate, Nadolol, Pindolol, Propranolol and Propranolol LA. Also OMAP is adding Avinza and removing Kadian from the Long Acting OPIOID class.

[A-083] Allison stated that in the Proton Pump Inhibitor class, the only drug that will be available is Prilosec OTC and all the others will be removed. Dr. Weaver asked how it works with Prilosec OTC being scarce? Allison stated that OMAP has sent a letter to the pharmacies notifying them OMAP is aware there is some spot shortages of the Prilosec OTC, but overall haven't heard a lot of problems so far and have asked them to

contact the provider and have them prescribe the next least costly drug which is generic omeprazole. Dan Kennedy asked if this would be re-evaluated as more generic manufacturers manufacture omeprazole? Dr. Weaver asked if there was a reason for the shortage? Dan Kennedy did not state a reason that he knew of.

[A-106] Allison stated that since the last meeting in April, OMAP has eliminated co-pays for the people enrolled in the Standard population, which was a result of litigation effective June 19<sup>th</sup>. She stated there are still co-pays for the OHP Plus population. She clarified that the co-pays also applied to medications.

[A-128] Dan Hartung, Pharmacist, OSU College of Pharmacy, presented survey results of OHP providers on their knowledge and attitudes of the PDL program. Dan stated it was faxed out as a 2 page survey in mid-April to the top 341 prescribers by cost. Dan referred them to the handouts in the packet. He stated they received 139 responses, which was approximately a 40% response. The majority of prescribers were in Multnomah and Jackson counties and the majority were in the higher density counties in the State of Oregon. The majority of prescribers were certified Internal Medicine or Family Practice. Dan referred them to the survey questions in the handouts. He stated that 63% said they were familiar with the PDL. In response to what they considered the largest barriers to using the PDL, they indicated that individual patient factors and just general awareness. In response to what tools the OSU College of Pharmacy could do to support educational efforts, the response was mostly to have a pocket card. In response to the question asked about specific agents selected by the evidence-based review, the results indicated they felt the selections were insufficient to meet patient needs in NSAIDs, Urinary Incontinence and Oral Hypoglycemics. The feedback indicated that there was misunderstanding of how the Oral Hypoglycemic class was characterized as they thought that metformin should have been included.

[A-224] Dan indicated that the key findings they gleaned from this survey is that a sizeable portion over 30% indicated they had no awareness of the state's evidence-based PDL. Of those who indicated they were aware the majority only indicated minimal familiarity. Awareness was identified as a barrier to using the PDL. Roughly a third of respondents indicated that individual patient factors were the major reason for not adhering to the PDL. The pocket card received the highest score for usefulness. A frequent but unsolicited comment was that they felt having a PDL available on some sort of Palm device such as Epocrates would be very useful. Again, NSAIDs, Urinary Incontinence and Oral Hypoglycemics were indicated as drug selections that were least likely to meet the needs of their patients.

[A-247] Dr. Baumeister asked if Dan could be more specific about individual patient factors? Dan didn't recall what they were specifically and didn't recall they were notable or that they were due to intolerance, etc.

[A-260] Dr. Weaver thanked Dan for his work on this and that she was impressed with the return rate of the surveys. She asked in regard to the NSAID class that they didn't feel the selection met their patient's needs, if there were any comments on whether it

was COX-2 Inhibitors? Dan recalled that there were some sporadic comments. He said he recalled that most comments were on the Oral Hypoglycemic and that metformin was not included. Dr. Weaver recalled that the subcommittee did discuss whether to include metformin but it is a totally different class. Dr. Weaver stated she was surprised at the UI response as the drugs are not that expensive. Dr. MacKay stated that it looked as if the # of choices was the factor here as these 3 classes had few choices, UI only had one choice, whereas the other classes had numerous choices and they seemed satisfied with those classes.

[A-306] Dr. Shaffer asked if there was an inverse relationship between their preferences and effectiveness as things such as patient order change forms and group educational sessions may be more likely to change prescribing behavior, which are more invasive so they may say they would take a pocket card, but wonder how effective that is.

[A-313] Dr. Weaver stated that she had been interested in the past looking at EPocrates and there may be renewed interest since it seems more doctors are using PDAs for the PDL and may be a way to attract more users.

[A-327] Paul Tiffany stated that he appreciated the survey and that it was significant to him that 76% indicated no or minimal familiarity with the PDL. He felt it showed that you could have whatever you want on a PDA but if they don't know about it or are not familiar with it, what good does that do. Paul stated he continues to be concerned about the education of those who prescribe these drugs and where do we go from here?

[A-341] Dr. Weaver stated that OHPR has sent a letter from various physicians in state government, including Dr. Goldberg, Dr. Turek and others, offering education. She stated that her participation addresses the pharmaceuticals. The letter was sent to 86 entities, e.g. IPAs, hospital staff, big clinics. So far they have had 2 tentative responses.

[A-365] Kathy Ketchum, RPh, OSU College of Pharmacy gave an overview of the baseline data, which was included in the packet. Kathy stated that this was the first prong of a several-prong education approach started back in March/April. She stated they responded to the survey and gave them a pocket card, which went out to 300 of the high volume OHP prescribers, which included a prescriber report that indicated this individual prescriber's rates of adhering to the list compared to their peers, on the average, which went out in May. She stated that this general report was sent just as information for baseline. She stated that this past week they started the targeted intervention. The sample in the packet shows Urinary Incontinence drug report individualized for each prescriber sent out to the top 130 prescribers of these drugs, which involved about 400 patients. They general information is on the front sheet and after that there will be a prescription form that facilitates the change to the lowest cost option for each patient. The process involves the prescriber evaluates the patient and determines if the change is okay, they fax this back to the OSU School of Pharmacy, we would notify the patient and send this on the pharmacy for filling. So far they have 70 to

100 positive changes so far in two days. She stated they would have a series of these with each class. They will do a general report quarterly or every six months so prescribers can track the change over time.

[A-413] Dan Kennedy asked if they had given a heads-up to the pharmacy community of these? Kathy said they are similar to what is used by Care Oregon and have run each form by the Board of Pharmacy for legal review. She asked if Dan saw anything of concern? He stated he did not but wanted to make sure the pharmacists knew what this was as they see a lot of stuff every day. Kathy stated that they will fax it back with a cover sheet that explains the program. Dr. Weaver asked what the period of time is that they can prescribe and Kathy responded they can write a Rx for as long a period as is legal. Dr. Shaffer asked if the prescribing pattern report given to the providers were informing providers of their adherence to the plan drug as a whole or was it adherence to the lowest cost? Kathy stated it was to the lowest cost. Dr. Shaffer thought it should be clarified, as it doesn't show how a provider is adhering to the PDL but is more educational focused on the lowest priced choice in the PDL. He felt the 2 lists didn't quite match as far as what feedback is being given back to providers. Kathy stated that they struggle with the list changes over time, whereas the lowest cost options generally stay there and so wanted something more stable but would be willing to entertain other ways of presenting that. She stated that because the list changes over time it is hard to monitor adherence over time. Dr. Shaffer stated it depends on what they are trying to educate the providers in. He stated that if you really looked at the details of the feedback that they were given, you could learn which of the drugs is the lowest cost and modify their prescribing, but it's just a question of how many providers are going to spend the time to do that and the quicker you can extract the information the more effective it would be. Dr. Shaffer stated he was concerned that a lot of people don't read it in detail to get that information and what can be done about that? Kathy asked if Dr. Shaffer had a suggestion for the next one that goes out probably in September/October. Dr. Shaffer suggested that there may be an advantage to giving providers feedback on their overall adherence to the PDL. Dr. Weaver suggested a separate column. Kathy Ketchum stated that it then gets into the simplicity vs. complexity issue.

[A-469] Dan Hartung stated that when this was initially started Prilosec OTC was not the benchmark drug at the time and so struggled, as they really wanted to push that because that was the cheapest of the PPIs vs. using the benchmark drugs. Then they compromised and chose the least expensive of the low cost options..... Kathy Ketchum stated it's all about where you draw the circles and the circles change and this makes it difficult. Dr. Shaffer stated overall that is the idea to get prescribers to prescribe the lowest cost of the alternatives if they are all equally effective and that was good.

[A-490] Kathy Ketchum stated the other piece she was presenting was in response to the HRC request regarding how they would evaluate this educational effort. She directed them to graphs in their packet. One lists the 2004 YTD PMPM (per member per month) for OHP Drug List and the other is an adherence rate with all the drugs on

the list as defined on 8-1-04. She noted that the overall class of PMPM is \$17 and they run currently at about \$100 overall so this is 17% of total cost. The other one shows adherence rate in each class and again this relates to how many drugs are on the list in each class. Overall there is about a 68% adherence rate to the current list. Dr. MacKay asked what the generic usage rate was? Kathy Ketchum stated it was about 62% overall but it is skewed by the mental health carve out, which is quite respectable for a Medicaid program.

[A-536] Paul Tiffany asked for clarification on the first graph of PMPM what percentage is the cost? Kathy stated it is about \$17 PMPM for PDL and the total cost is about \$100 PMPM. Dr. Weaver asked what portion of the \$100 is mental health? Kathy Ketchum stated it is about 50%.

#### **4. Report from Statin Subcommittee**

[A-567] Terri Bianco, PharmD, Chair, gave the Statin Subcommittee Report. Dr. Bianco stated that this would wrap up her involvement with the subcommittee and expressed her appreciation for the opportunity to participate in this important process. She stated it had been very enlightening and informative on many levels and congratulate the commission emphasizing the evidence in this process and its decision-making which you have received a great deal of national recognition and a great deal of that positive.

[A-583] Dr. Bianco summarized the subcommittee's new findings and revisions of the report, which are highlighted. She noted increased information about the newest statin, rosuvastatin, to reduce LDL-c, and that the report was modified to include this agent for the amount of LDL-c lowering it can achieve. She stated that in the original version of this report KQ2 regarding the correlation between LDL lowering and risk reduction of clinical outcomes, at the May 5<sup>th</sup> meeting were informed that this question had been deleted as a KQ in the EPC report. After much discussion the consensus was to delete it as one of their KQ also primarily because they felt it lacked clarification and didn't necessarily express the original intent of the question. She stated that the subcommittee requests that consideration be given to the addition of the following KQs, which more specifically reflect the information that was felt to be needed to assess future Statin drug choices. The new KQ is: "What is the correlation between the magnitude of LDL-c lowering and the risk reduction for cardiac outcomes? What is the correlation between LDL-c lowering and adverse effects? Can the benefits and risks from statins as a class be extrapolated to a newer statin that has proven LDL-c lowering capability but has yet unproven cardiac outcomes?" She stated in other words, as more potent statins become available and the goals for therapy become perhaps more aggressive, clinicians need to know the evidence that supports both the efficacy as well as the safety of the available statin agents.

[A-620] Dr. Bianco stated the new KQ2 discusses the comparative ability of statins to raise HDL. She stated this KQ was new to this report and the subcommittee agreed it was pertinent and to adopt it as one of the KQ. She further stated the subcommittee

concluded by consensus that all statins achieved similar HDL increases when compared at equal potent doses.

[A-629] Dr. Bianco stated that KQ3 relates to the comparative ability of statins to reduce the risk of cardiovascular morbidity and mortality and the summary statement was revised to reference new data comparing atorvastatin and pravastatin and continued to acknowledge those drugs for which outcome data is available.

[A-639] Dr. Bianco stated that KQ4 regarding differences in safety or efficacy in different demographic groups, the subcommittee felt there was no significant new evidence that would warrant a change in the summary statement other than some minor wordsmithing regarding efficacy in racial groups.

[A-642] Dr. Bianco stated that KQ5 regarding differences in safety in special populations, there was little new clinically significant evidence, which would indicate a need to substantially alter the conclusions. She stated they did point out that rosuvastatin is an additional agent that is not metabolized through the cytochrome P450 system, which is the metabolism route by which significant adverse drug interactions can occur and that statement was added.

[A-653] Dr. Bianco stated that in the course of conversations none of the KQ addressed the issue of comparability of adverse drug effects in general, i.e. in non-special populations, so the subcommittee recommends that this KQ be added: "What are the comparative incidence in nature of adverse effects of the different statins". She stated the subcommittee felt that the update information provided did not warrant any additional conclusions be added or alterations to existing conclusions. She noted that the conclusion sentence 3. related to the deleted KQ3.

[A-674] Paul Tiffany asked for clarification that no changes were made to the previous conclusion even though there were changes to the KQs? Dr. Bianco stated they did eliminate 3. in the final conclusion box. She stated that the findings for the new KQ regarding HDL didn't indicate significant enough findings to modify the recommendations. Dr. Weaver stated that these are Oregon's proposed statin KQ modifications and will be for the next report. Paul Tiffany reiterated his question that the elimination of a KQ and the addition of another didn't result in more changes to the final conclusions? Dr. Bianco again stated that the sentence in the final conclusion in response to the eliminated KQ was deleted. Paul Tiffany said he raises this due to all the comment about changing KQs in the review process and is concerned that they follow the proper process. Dr. Weaver stated the new KQ was added in the EPC report and reported in this report but the subcommittee didn't feel that there was any clinical outcomes that you could separate out from raising HDL because at the same time they raise HDL they lower the LDL-c and nobody has been able to correlate what that means clinically and is something that the subcommittee will continue to follow and future research may be able to tease that out. She stated it is in the report but didn't change the final conclusion. Paul Tiffany questioned that the discussion took place at the subcommittee level and among staff and doesn't recall discussing it at HRC and asks if

there was any input from the industry? Paul Tiffany stated he recalled a lot of discussion on KQ in a previous HRC meeting from the industry. Dr. Weaver and Dr. Bianco both stated they did not recall any persons from the industry bringing it up during the public comment period. Dan Kennedy stated that as a subcommittee member one of the problems with the original question #2 is when you read it very closely it seemed so ambiguous that even the members who had been part of the subcommittee for the past two years weren't exactly sure what they were asking and stated that the proposed modifications are more of a clarification and in some cases a clarification with new information that is becoming available and so the questions will provide better answers overall.

[A-751] Diane Lovell confirmed that Paul Tiffany's concern was to ensure that the discussion happened in the public meeting and if anyone had an interest in not modifying that they had an opportunity and that she understands the answer was yes. Paul Tiffany stated that the discussion they are having now about changing the KQ for next time is appropriate and just questions whether that same process took place on the other changes? Dr. Weaver stated it wasn't as far developed as it is now and that the process she would like to follow now was to bring proposed changes to the KQ right at the time the subcommittee is wrapping up and look ahead at the next one. She stated that then having the opportunity to bring it back to the HRC and therefore get some direction so when they have the conference call on August 5<sup>th</sup> with the Center then she will have some direction to give and Oregon will be able to participate. That also gives the industry at least two opportunities to comment both at the subcommittee level and here. Dr. Weaver stated that in the answer to the question of did it happen that way, things were changing and so this is the way we want to do it. Dan Kennedy stated that these modifications are proposed and there is still opportunity for comment. Dr. Bianco stated that the ones that are in the document now as it stands here today, those revisions took place within the context of the subcommittee. Paul Tiffany asked if the industry didn't comment on the change at the subcommittee and Dr. Bianco stated that she didn't recall that they did. Dan Kennedy stated that it was as ambiguous to the subcommittee as it was to all. Paul Tiffany again asked for clarification that no change what they already had? Dr. Weaver stated it was a level 3 report because of new information and a new drug, rosuvastatin, and because there were some significant papers but ultimately did not change the final conclusion. Dan Kennedy commended Terri Bianco for the fine work she has done for the subcommittee for the last two years as it has not been an easy subcommittee and can vouch for the fact it wasn't an easy subcommittee.

[A-821] Trish McDaid-O'Neill, Regional Account Director, Astra Zeneca, gave public comment. She stated that in regard to a reference in the Statin report on page 8, paragraph 3, regarding the STELLAR trial, the reference of 80 mg be removed as it is not an available dosage. She stated the maximum dose of rosuvastatin is 40 mg or that a qualifier be put in that 40 mg is the maximum dose available. Dr. Bianco stated that the subcommittee did agree and thought all references to 80 mg had been removed. Dr. Weaver said there was a typo and it had said 40 mg and did get it changed to 80 mg as it was stated in the EPC report, but Trish is asking that the sentence be removed and

Dr. Bianco thought it had been decided to do that. Dan Kennedy, Dr. Bianco and Dr. Weaver agreed that the sentence should be removed and appreciate Trish bringing it to their attention. Dan Kennedy stated that the point the subcommittee wanted to make was that the more potent statins pose the potential risk of higher adverse affects. Paul Tiffany asks Trish if removing the entire sentence would take care of her concern? Dr. Baumeister asks what the purpose is of the highlighting? Dr. Weaver stated that anything that is new since the last update is highlighted. She also stated that anything that is deleted is lined out and that maybe the final version will not reflect the lined out portions.

[A-966] Dr. Weaver stated she has been putting footnotes and references in the reports and asked if that was helpful. Dr. Baumeister stated it was very helpful.

[B-010] Dr. Shaffer asked if by adopting the Statin report did they approve the proposed new KQ or is that a separate discussion? Dr. Weaver asked if the commission could address that at this meeting.

**[B-019] Action: All members present agreed to accept the Key Questions as presented at this meeting. No public comment was given.**

[B-027] Dr. Weaver stated she had sent the proposed KQ changes to AstraZeneca and they were in agreement with the direction of the KQ and for them the pertinent question was “is this a class affect you can extrapolate to a new drug” because their drug is in that situation where they have intermediate outcomes with Crestor.

[B-030] Dr. Baumeister read the Key Questions to confirm all members understood the KQs. Dr. Weaver stated the KQ 6 had been asked in every class but now the July 13<sup>th</sup> NCEP guidelines are going to qualify three times as many people to take statins and so the subcommittee felt it was very important to make sure that even lower risk groups be followed to make sure they are not having adverse events. Dr. MacKay asked for clarification of the language that is highlighted. Dr. Weaver stated the KQ that was taken out is similar but is different in regard to magnitude of LDL-c lowering and reduction of cardiac outcomes. Dan Kennedy stated that 2a and 2b are attempts to better clarify.

[B-076] Dr. Shaffer asked if KQ3 could be answered by a systematic review of the evidence? Dr. Weaver stated the subcommittee felt it was a judgment call in case they were asked to make that judgment the next time. She stated when there are 5 out of 6 statins that all eventually prove they affect cardiac outcomes when they lower LDL-c, at what point do you say that is a class effect? She stated there may not be any information on that and asks the EPC if they think they can get information on that? Susan Carson, EPC, responds that it is more a question of.....and didn't recall this question being discussed at the subcommittee. Dr. Weaver stated that Jim Slater brought it up at the meeting. Dan Kennedy stated that the discussion at the meeting stemmed around if they have evidence that LDL-c lowering goes in conjunction with cardiac outcomes and moves toward greater LDL-c lowering capability of more potent statins, then are we really quoting the obvious? He states when you have 21 out of 21 statins that are shown to have good cardiac outcomes with good LDL-c lowering capabilities, at what point do you say this looks like a class affect. Dr. Shaffer and Dr. MacKay stated it would be a judgment call by the subcommittee. Susan Carson stated she couldn't think of a trial or study design that could answer that question. She stated she didn't think it would be possible. Paul Tiffany asked if the EPC would state they couldn't deal with it? Susan stated yes. Paul asked if the question

should be here if the EPC can't address it. Dr. Weaver stated the subcommittee didn't have an in depth discussion about it and don't know if there is any information out there and if it is left in there it will prompt discussion at the conference call but would be nice to leave it in in case there is information out there.

[B-132] Dr. Baumeister stated they have come full circle as initially they were focused on clinical outcomes and heard Dr. Helfand testify here and defend clinical outcomes and have had a lot of controversy about that issue. He stated in the early days of obtaining double-blind controlled studies and focusing on the clinical outcomes proving that one drug worked because it seemed to have beneficial effects on preventing cardiac events because it lowered LDL-c and another drug came along and just lowered LDL-c but they didn't do any head-to-head comparisons and they didn't do clinical outcomes studies. He stated that testimony was given that they were being unfair to these drugs because they did lower LDL-c and these other drugs lowered LDL-c and you didn't have as many MIs and now we are saying it is okay to extrapolate. He states they lower LDL and we just don't know what else they do. Dan Kennedy agreed and why they wanted to keep this on the table was this PROVE-IT study that compared atorvastatin and pravastatin head-to-head found that basically by decreasing the LDL-c that you had better outcomes and we just wondered at what point do you then make that leap. He stated it was an intricate controversial discussion very early on in the process. Dr. Weaver stated they are posing the question to see if they have guidance to stay with that from the HRC? Diane Lovell stated she felt they should stay the course and stick with evidence and outcomes and in the future if the subcommittee wishes to deviate it would be helpful if it was teased out in the questions and presented as a specific request of the subcommittee and then the HRC can decide whether to include it or whether inquiring minds want to know let them ask but still not part of the report. She stated it could have been missed and appreciates the diligence in noticing that and pointing out that it was different than KQ in the past. Paul Tiffany agreed and thanked the committee for teasing it out. Dr. Baumeister recalled the long testimony here about going back to the laboratory and what had been demonstrated in the lab and should accept that and we decided we didn't accept that and feels they should stick with clinical outcomes

[B-200] Dr. Shaffer suggested that if there was a way to include the statement of #3, not as a KQ, but as a topic to be addressed in the review for the reason that he doesn't want to miss what truly is helpful for patients by sort of sticking to their guns of clinical outcomes. He states that in the cholesterol lowering business the NIH guidelines bought the argument that LDL-c lowering is beneficial in reducing cardiac events, so for the HRC not to accept this argument is going against some trends. He states that there is also some precedence for including laboratory intermediate markers with the diabetes agents so haven't stuck to clinical outcomes 100% so think it would be best to address this question somehow. Diane Lovell stated her objection isn't asking the question but its potentially including it as a KQ and think there should be distinction between that question and the KQs and doesn't oppose the pursuit of information. Dan Kennedy states he understands this represents a fundamental shift and doesn't think there be much of a problem dropping #3 as a KQ as long as there was some discussion about that proposal at some point, and think the consensus of the subcommittee that LDL-c the writing is pretty much on the wall and to ignore that seems irresponsible. Dan Kennedy proposed elimination of KQ3 as long as it is addressed in a future meeting of all stakeholders including the EPC. Dr. Weaver stated that while some of the reports can be as long as a year in being revised, the statins are slated to be 6 months and so will be revisiting this often. There was discussion and agreement that staff will instruct the subcommittee the next time they meet to determine what information is available in connection with this question even though it is not a KQ.

**Action: All members present agreed to accept the proposed Key Question changes minus KQ 3.**

**[B-001] Action: All members present agreed to remove the sentence in question and approve the report as amended.**

*Handout: Statin Subcommittee Report, Update #2*

## **5. Report from Standing Update Committee**

[B-308] Dr. Weaver stated that Dr. Labby was not able to attend and she will give the reports on his behalf. Dr. Weaver gave an overview of the appointment of the Standing Update Committee and its membership.

[B-323] Dr. Weaver directed the HRC to the NSAIDs Subcommittee Report Update #2. She noted that there were no new drugs added. She noted that there was minor new information but that no changes were made to KQ1 consensus statement. She noted that under KQ2 the word “other” is highlighted. She said it previously said “selective and non-selective” and it was pointed out by pharmacy colleagues that you can’t separate this out so the word “other” was substituted. She noted that the only change in the KQ2 consensus statement is the word “other” as explained. She stated no changes were made to KQ3 consensus statements. Dr. Baumeister stated that the word is not getting out about COX-2 and not NSAIDs. He stated the doctors just don’t get the word. He stated there is an education process that is needed. Kathy Ketchum stated that NSAIDs is their next target and will work on that message. Dr. Weaver talked about the ADVANTAGE trial outlined on page 13 as not being significant enough as it was not long enough. There were no changes in KQ4 or the conclusion statement other than substituting the word “other”. Dr. Weaver stated that a couple articles have been recently published and will be incorporated into the next report.

[B-428] No public testimony was offered

**Action: All members present approved the NSAID Subcommittee Report #2.**

[B-432] Dr. Weaver presented the ACE Subcommittee Report Update #1. Dr. Weaver stated that Dr. Crispell attended the meetings as a consultant and the committee met twice on this topic. Dr. Weaver noted the new findings found no new ACE Inhibitors. Dr. Weaver explained that on page 13 in the text right above the box says “heart failure” whereas before it said CHF, which is misconstrued sometimes as congestive heart failure or chronic heart failure so it was changed to just heart failure and this was changed in the conclusion statement also. Dr. Weaver went through the report and noted that no changes were made to any of the consensus statements.

[B-505] Kathy Ketchum gave testimony and noted that “≥10” mg for Ramipril was added and needed to be highlighted. No other public comment was taken.

**[B-517] Action: All members present approved the ACE Subcommittee Report Update #1.**

*Handout: ACE Subcommittee Report Update #1*

## 6. Process Update

[B-527] Dr. Weaver referred the commission to the Process document in their packets. She stated that this document was being brought back to finalize their recommendations from the previous meeting. Dr. Weaver directed them to the first page and discussed how changes to the KQ will be discussed by the subcommittee as they finalize each report. Diane Lovell asked what “standardized” KQ meant? Dr. Weaver explained the three basic questions in each KQ document, i.e. efficacy, safety, effect on special populations.

[B-561] Dr. Weaver directed the commission to page 2 and stated that a revision could be made to drug classes being reviewed once per year and changed to read “at least” once per year as some will be reviewed more often than once per year. She stated that Statins will be one of those that is reviewed more than once per year. Dr. Weaver outlined the amount of input from the original subcommittee, public and the HRC. She next reviewed the Update Committee section.

[B-611] Dr. Goldberg stated that the main issue is that everybody understands the interactions between all the people involved in this process. Dr. Weaver stated that they tried to make this a proactive, rather than reactive, to what is going on and her job is to keep the commission informed of all these things.

[B-627] Dr. Baumeister comments on local autonomy and where to go with the whole process. He stated it was an issue before. Dr. Weaver stated that as with Statin KQ the commission has input on what direction they want to go.

[B-634] Paul Tiffany asked where the discussion of modifying KQ as they did today fit in this process? Dr. Weaver explains that if it is a category 3 the subcommittee does the update, if it is a 1 or 2 the Standing Update Committee does the update. She stated that what they did today falls under the 5<sup>th</sup> box under the Proposed “Update Review”. Dr. Baumeister noted that it says draft until it is finalized by DERP and then if the HRC’s KQ are not included, Oregon may work with EPC. Dr. Goldberg stated, e.g. Oregon will give input that does not have question 3 and they may choose to include 3 as a KQ. This group, however, has decided that you won’t but that information will be in the report and this group could use it or not use it. Likewise, if there are some KQ that the HRC particularly wants addressed and they are not addressed by the larger group, then we can have the EPC address them as Oregon’s own process and bring that information back to the HRC. He stated that the idea is to basically collaborate when there is absolute consensus but allow some autonomy when there is additional information that we would like or if there doing additional information that is going to be fine by us.

[B-699] No public comment was heard.

**Action: All members present approved the Process Document with the one modification of adding “at least” to read “Drug classes reviewed ‘at least’ once per year.**

*Handout: PMPDP Process*

## 7. New Subcommittee Rosters

[B-711] Dr. Weaver introduced the new Subcommittee Roster for Alzheimer and Inhaled Corticosteroid. She noted that she did not have enough information to put the volunteers for the Anti-Platelet group. She gave an overview and asked for approval of the members that were in *italic* as they had gone through orientation and had completed all forms necessary.

**Action: All members present approved the roster of the Alzheimer subcommittee subject to completion by Dr. Devarajan of necessary documents.**

*Handouts: Subcommittee Rosters*

## **8. Status of Drug Class Reviews**

[B-769] Dr. Weaver presented the Alzheimer and ICS Key Question documents and stated they were more for information. She stated that the Alzheimer Subcommittee had a chance to respond to these and had a discussion with the Center for Evidence-based Policy (Center). She stated that the kind of things that the Alzheimer Subcommittee wanted included were the treatment of behavioral disturbances and the effect on the caregivers, specification of subpopulations that identified early mild Alzheimer disease as compared to moderate or severe because there seems to be a real difference in how these drugs work. She asked Kathy Ketchum to comment as the interventions have two different classes of drugs within the same group which are Aetylcholinesterase Inhibitors and Memantine. Kathy Ketchum stated Memantine is the newest drug to treat Alzheimers. Dr. MacKay stated its indication is for severe Alzheimers patients.

[B-819] Dr. Weaver presented the Inhaled Corticosteroid Key Questions and stated they were the standard questions. She stated the input Oregon gave on this was to make sure it was both adult and pediatric outpatients with asthma. Dr. Weaver asked Kathy Ketchum if more of these drugs are going to be in different forms that might affect the market? Kathy Ketchum stated that in Inhalers there has been a phase out by the FDA of propellant and moving to those without that. Dr. Weaver asked if those will be mostly brand names and Kathy Ketchum stated yes and responded yes when asked if they were more expensive.

[B-870] Dr. Baumeister asked how long the Alzheimers had been in the works? Dr. Weaver stated it had just started. Dr. Baumeister stated he wasn't surprised that they heard from Allison Knight that they were going to do Alzheimers and Anti-Platelet and NSAH and now we are presented with the KQ already formulated for the Alzheimers. Dr. Weaver stated it was because the Governance group decided that earlier and so the Center and EPC are moving along on that and so Oregon did have a say at the Governance meeting about this. Dr. Baumeister asked if they had been discussed here? Dr. Weaver stated that part of the problem was that HRC didn't have two meetings and these things change every month and if there isn't a meeting it gets behind. Dr. Baumeister stated that it appeared the HRC had been taken out of the loop? Diane Lovell said it sounded like the process bypassed them as they didn't meet. Diane suggested that staff keep them informed by another method if there is no meeting so they are kept up-to-date. Dr. Baumeister stated he had been struggling against this for a long time as there is staff and volunteer people on the Commission and the volunteers on the Commission should know what is happening all the time. Dr. Baumeister stated it was not a big deal. Dan Kennedy stated he agreed and that his response to NSAH is that even a sliver of the pie to this population? Kathy Ketchum stated that they are getting so far down in their classes right now that it is one of the higher ones.

[B-926] Dr. Baumeister stated this has the danger of becoming a bureaucratic process that he has struggled against ever since he has been on this Commission. He stated it is leaning more and more that way and would like to bring it back so the Commission is in charge of this thing. He stated that for staff it is their work and the Commission does other things and then come here once in awhile and it is a balance and is important and had had his own difficulties with OMAP as everyone knows. He states that OMAP is a government agency and they have a certain agenda and as a practicing physician with a patient population and colleagues to whom

he has to sell these programs, he has an agenda and they are not always in sync. He states that OMAP thinks they can go out and educate docs on how they can comply with this program they got another thought coming. He stated you can get them all a hand held EPocrates but as long as big brother is looking over their shoulder and telling them how to prescribe drugs they are not going to like it. So it has to be a grass roots thing and come within and they have to believe in this program. He stated for them to believe in it the HRC has to believe in it. He stated then it starts going from OMAP to you, to big brother or somewhere else, whether its John Santa or who cares its going to lose some of it's influence within the state. He stated that so far you depend on influence, you don't have a lot of authority and as long as you deal with influence without authority you got to be pretty...have a lot of influence and that is what is wrong with this program and why there is not more compliance. He stated you either have to have a hammer, a big stick or a tasty carrot.

{Tape 2 – A – 001} Dr. Baumeister stated that trying to sell it to the OMA is one of the biggest hurdles and states he is sensitive to these things and it needs to be taken into consideration for the future. Dr. Weaver commented on the difficulty of getting a quorum and having meetings during this summer and the process moves a lot faster than it did before. She stated it used to be that you could have quarterly meetings and cover most everything. Dr. Baumeister stated he didn't think it needed to move that fast here. Dr. Weaver stated it does if you want to have input on the decision-making because she can't control what the other 15 states are doing. She stated she can keep the HRC informed and if they could meet and do it ahead of time they can be ahead of the wave. She stated that the process is different in some ways than before and she is trying to make it fit as best as possible and have the HRC continue their leadership role. Dr. Baumeister stated it is a red flag. Dr. Weaver stated that Diane's suggestion is a good one in that if HRC is unable to meet a news brief goes out but cannot take any votes but can get the information out.

[Tape 2 – A – 024] Diane Lovell stated that it would be helpful to see how the meetings and HRC work tracks with DERP so they can say what they are going to be working on and here are HRC's so they can understand the relationship and anticipate that. She asked if they publish Minutes to the participating organizations? Dr. Weaver said they do not produce Minutes but a number of organizations including Oregon has requested a firm timeline so that we know which drug group key questions at which meetings. She stated they are to the point now where they think they can come up with this. She stated that would be very helpful and can then correlate so HRC is ahead of it but that she has been dealing with the unknown. She stated it has been getting better and is a developing process and is certainly more complicated than it was before.

[Tape 2 – A – 041] Dr. Shaffer stated that HRC had a process that they had to develop over a couple years and now there is a more complicated multi-state process that we are having to fit ours into, so the challenge is in order to maintain any sort of autonomy maybe for the benefit of the State of Oregon of being involved in the bigger organization and would be more effective in Oregon if we are involved more than state bureaucrats. Paul Tiffany asks if that is the way the law reads and that it is a Commission responsibility as opposed to staff, staff can give some recommendations, but Alzheimers Key Questions don't go anywhere unless the HRC approves them? Paul states that Frank has a very good point.

[Tape 2 – A – 060]

No public testimony given

**Action: All members present approved the Alzheimer and Inhaled Corticosteroid Key Question documents.**

## 9. HRC Membership

[Tape 2 – A – 073] Dr. Goldberg stated that they had some suggestions from people on the Committee and are soliciting replacements for the vacancies. Dr. Weaver stated that they also need to reappoint Wally, Dean and Dan and soliciting members for the others. Dr. Goldberg stated that the cake is in recognition that this is Dr. Baumeister's last meeting. Dr. Goldberg stated it is not Diane's last meeting. Dr. Goldberg and Dr. Weaver presented Dr. Baumeister with a plaque and complimented and thanked him for all his years of service and contributions to the Health Resources Commission. Diane Lovell also thanked Frank for being able to work with and learn from him all this time as he has been the champion of this commission.

[Tape 2 A – 197] Dr. Baumeister gave some history of the Commission. He stated that he would continue to be a spokesperson for the program and promote the program and thanked everyone for their kind comments.

### Meeting adjourned.

#### Handouts:

- a) Agenda
- b) 4-16-04 Minutes
- c) Survey Result documents from OMAP
- d) Baseline data from OMAP
- e) Statin Report Update #2
- f) NSAID Report Update #2
- g) ACE Report Update #1
- h) PMPDP Process document
- i) New Subcommittee Roster
- j) Alzheimer Key Questions
- k) ICS Key Questions
- l) HRC Membership

**MINUTES**  
**HEALTH RESOURCES COMMISSION**  
**August 20, 2004**

**Members Present/Phone:** Chair, Walter Shaffer, MD - Vice-Chair, Diane Lovell - Paul Tiffany - James H. MacKay, MD - Mark Yerby, MD.- Elaine Dunda - Dean Haxby, PharmD

**Members Absent:** Steve DeLashmutt, MD - Dan Kennedy, RPh

**Staff Present:** Kathleen Weaver, MD, HRC Director – Betty Wilton, HRC Project Coordinator

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**1. Call to Order and Roll Call**

[A-001] Meeting was called to order by Vice-Chair, Diane Lovell and roll call taken. Diane asked for nominations for a new Chair. Dr. MacKay nominated Dr. Shaffer. The motion was seconded and Dr. Shaffer was elected unanimously as Chair of the Health Resources Commission. Dr. Shaffer asked for nominations for Vice-Chair. Dr. Weaver stated that the Governor is sticking to two terms for all commissions. Diane Lovell stated that her term has expired and she has served several terms and it is time for her to step down but did agree to stay until a replacement has been appointed. Diane nominated Paul Tiffany for Vice-Chair. Dr. Weaver stated that the Governor's office is working on the new appointments for the current vacancies and asked for recommendations.

[A-052] **Action:** Dr. Shaffer was unanimously elected Chair of the Health Resources Commission. Paul Tiffany was unanimously elected Vice-Chair and agreed to serve when Diane leaves.

[A-008] Dr. Shaffer talked briefly about this being a challenging time for the commission losing several long term members but suggested looking at this as an opportunity to get some new ideas, new interests and how the role of the commission is evolving due to the Center involvement and that there are currently 17 subcommittees and to look forward to opportunities for the commission to be involved in other aspects of the way the State of Oregon looks at publicly funded healthcare delivery.

**2. Approval of Minutes**

[A109] **Action:** The 7-16-04 Minutes were unanimously approved.

**3. OMAP Update**

[A113] Allison Knight, OMAP, asked the Commission to undertake the review of Bisphosphonates for Osteoporosis. There was discussion about how much benefit would be derived from reviewing this class. It was suggested that the benefit may not be seen until further down the road when new drugs enter the market and in view of what happened with the Estrogen class regarding the impact on osteoporosis. However, the review would be limited to two bisphosphonate drugs the FDA approved for treating osteoporosis.

**Action:** The Commission unanimously agreed to accept review of the Bisphosphonate drug class and review the draft Key Question document and determine at a later date when to put a subcommittee together.

[A-245] Allison stated that the Plan Drug List will be revised in the ACE and NSAID drug class effective November 1, 2004, ACE will now include Analapril, Aceon, Captopril, Lisinopril and Indo-methacin. The NSAID drug class is also being updated to include Naproxen, Ibuprofen, Proxicam. Allison stated that OMAP did implement the redefined OHP Standard Benefit Package on August 1, 2004. No questions were asked.

[A-265] Kathy Ketchum, OSU, gave a preliminary report on the Preferred Drug List Educational Initiative that OSU undertook. She discussed the surveys that were sent out and the Change Form interventions. 412 change forms were sent out on the Urinary Incontinence drug class to 156 unique providers. They received 279 forms returned for a 68% response rate. Of those 235 changed to the preferred product. So, that is a 57% acceptance rate. Of note, this was one of the 3 classes in the survey that was identified as not something that would be acceptable for their patients. Of the ones that were not returned and didn't authorize a change 27% were identified as an inaccurate provider identified on the claim. The others said the patient was unstable currently and 16% said the patients had a previous failure on the preferred drug. These are rough numbers but stated it looks like OMAP saved \$21,000 per month or a quarter of a million per year, on just this one drug class. Kathy stated that surveys on NSAIDs went out and then next is PPIs.

#### **4. Report from Standing Update Committee**

[A-305] Nicole O'Kane, PharmD, presented the Calcium Channel Blocker report from the Standing Update Committee. Dr. O'Kane noted there were no changes to the questions or any of the conclusions of the report, but said they did spend the better part of two meetings talking about this report. She stated there was a presentation from the EPC and there were new findings but mostly in the label indication changes from the FDA, and additions to controlled trials that they had looked at before. There wasn't any information that encouraged them to change any of the recommendations. They did have some discussion about the new trials and how they could be compared and always learn more from the research people that have expertise in literature review. She stated that Dr. Kathy Crispell, a cardiologist, was consulted and she was very helpful in helping them review the information and would be joining the Standing Update Committee as a permanent member replacing Dr. Pettit who had to resign. Dr. O'Kane stated there were no major discussions from the industry or any controversial comment from the public. The only change will be in anticipating the future key questions. She stated they did discuss whether any of the key questions needed to change and it was decided that no changes were needed, but there will be a change in the way the EPC does their search to include more observational trials that were not included the first time around and will pick up the information about the short-acting CCBs and information about safety and the expert Cardiologist agreed that was a good idea.

[A-344] Dr. Weaver stated that there have been reports particularly with the non-dihydropyridines as a class and on page 4 of the CCB report, although there has been no change in the number of CCBs there has been a lot of change in the generics particularly under Diltiazem and most of these are going now to long-acting form.

[A-363] Dr. Weaver stated that she felt she was developing a more streamlined process and yet covering all the information. Paul Tiffany stated that he thought the process was working well and the people on the Standing Update Committee are really dedicated to doing this.

[A-373] Dr. Shaffer asked if the Standing Update Committee was concerned that some information had been missed. Dr. O’Kane stated it was intentionally excluded during the first review. The original subcommittee knew the EPC didn’t, in general, include observational studies because of the lack of quality. Kathy Ketchum stated that they do include observational studies for safety. This was an unusual circumstance where they excluded it because of the volume of the literature that they had to review. Dr. O’Kane stated they knew and it wasn’t a surprise and would be reviewed at a later date, which they will now be doing. Kim Peterson from the EPC stated it was correct that the literature was excluded because of volume, but the EPC will do it now. Dr. MacKay stated that the problem is that most of the studies are meta-analysis and subgroup analysis and not really a new study to demonstrate difference in side effects from the short and long-acting drugs so there are lots of studies but not that great.

[A-417] An Pham, PharmD, Reliant, gave public testimony. Dr. Pham asked for clarification on page 7 in “5. Adverse Effects” that states study is a controlled clinical trial of a least 6 months duration could be shorter than 6 months because drug interaction could be immediate.

[A-449] No other testimony was given. **Action: The commission unanimously approved the Calcium Channel Blocker report.**

## 5. Drug Class Updates

[A-455] Dr. Weaver asked the Commission to approve new volunteers as outlined in the New Subcommittee Roster handout. Dr. Weaver gave a brief overview of each new volunteer. Dr. Weaver stated that Dr. DeLoughery stated he would not speak for BristolMyerSquibb as they make an antiplatelet product. **Action: The following professionals were approved: Sumathi Devarajan, MD; Patrick Callahan, EMT; Marge Dettwiler, NP; Martin Johnson, MD; Michelle Murray, PharmD; Earl VanVolkinburg, MD, Thomas G. DeLoughery, MD; Linda Miller, RN; and Rick Tipton, RPh., with the expectation that Dr. DeLoughery will not speak on behalf of BMS.**

[A-582] Dr. Weaver presented the Calcium Channel Blocker Key Questions and stated the only recommendation from the subcommittee and update committee is that observational studies are included this time. Dr. Weaver stated that she thought it was a good idea that the length of the studies would not need to be 6 months or longer. Kim Peterson, EPC, stated that the EPC generally applies the 6 month duration to the observational study evidence because they are really relying on that body of evidence of long-term safety, so they do want to see the longer studies there, so the EPC input would be to adhere to the 6 months. Kathy Ketchum stated that having a minimum of having a long-term study doesn’t preclude us from collecting information in 24 hours. She stated they would not be excluding information at 24 hours by making the minimum a long term. Dr. Shaffer summarized that the 6 month studies would pick up the 24-hour reactions. Kim Peterson, EPC, stated that the participating organizations make the final decision—makers on the scope of work so Dr. Weaver would bring their strong feelings to that governance group as a recommendation. Paul Tiffany asked if this would add a whole bunch of new studies? Kim stated it would definitely increase the volume of the research. Dr. MacKay stated there are tons of 12 week studies because that is how the drug gets approved for the FDA, but the long term studies are what we are interested in for the clinical outcomes, efficacy and how people are reacting, dropping dead after 6 months or any time in between and so does support asking for long term studies and it would clutter up things to include the real short term studies. Paul Tiffany expressed concern that the workload asked of the EPC is manageable.

[A-675] Dr. Weaver presented the Oral Hypoglycemic Key Questions and stated they were presented to the Standing Update Committee at their last meeting on August 10<sup>th</sup> and they felt there were no recommendations to change the Key Questions but recommended deleting “adult” in the Inclusion Criteria in order to capture the pediatric population. Paul Tiffany recalled that someone was going to check into why the younger population was excluded in this review, as there had been a conscious decision to exclude the younger population. Dr. Weaver will raise the question at the Governance phone conference. Dr. Goldberg verified that these KQ were also sent to the subcommittees for feedback who have expertise surrounding this group of medicines. Dr. Weaver stated the recommendations were collated from all the subcommittees and presented to the Standing Update Committee. Dr. Goldberg reiterated that the subcommittees are not convened to just look at the key questions but instead they get emailed out to them, their input is solicited and considered at the Standing Update Committee, just so you know when it gets here you’ve had 2 group reviews and the original group who has specific expertise around this has had an opportunity to give feedback. Often times they have said no changes, but felt it was important for the Commission to fully understand all the input that is getting into these before being presented here at the Commission.

[A-760] Dr. Weaver emphasized that the grey shaded language was added by the EPC or by the DERP collaboration. She talked about what was added. There was discussion about why metformin was not included. Dr. Weaver will bring this up at the Center phone conference. Dr. Haxby suggested also asking about glitizones, all oral agents.

[A-838] Dr. Weaver introduced the NSAID Key Questions. These also were sent to the original subcommittee. The feedback from the subcommittee was presented at the Standing Update Committee meeting. There was a suggestion to replace “coxibs” with “COX-2” for consistency. It was also suggested on question 3, which was divided in two to identify medications used “acutely” or “chronically” as far as the safety or adverse effects. The Standing Update Committee suggested adding NSAID and Cox-2 Inhibitors/Cox-2 Inhibitors, because you can use an NSAID with an anti-ulcer or can use a Cox-2 Inhibitor with an anti-ulcer. Paul Tiffany stated that it clarifies the questions that the EPC is gathering and reporting on. These changes clarify the key questions to reflect that. Dr. Weaver stated that it was also raised by the subcommittee on question 4.5 regarding drug interactions and co-morbidities, what is the situation when you have low-dose aspirin plus an NSAID or a COX-2 Inhibitor as far as either cardiac or GI effects. So this would be a patient who has cardiac disease and is on prophylactic aspirin but then also has arthritis and is taking an NSAID or a COX-2 Inhibitor and what are their risks of having either cardiac disease or GI bleeding. This is getting complex and Dr. Helfand was going to look at a way to perhaps word that question if it were included. I think it certainly would be interesting to bring up during the conference call. Dr. Weaver stated that it was suggested to add Salsalate to the review. Kathy Ketchum stated it was an important alternative to be considered in this class because it does have some safety properties. She recommends including it in this class. Kim Peterson stated that the EPC agrees with this recommendation.

[B-001] Dr. Weaver continues review of the NSAID Key Question document. She states under serious cardiovascular events that hypertension, congestive heart failure be included, there have been some recent articles about congestive heart failure with these drugs. She stated it is a matter of refining the questions to ensure the evidence is captured in the tables.

[B-015] Dr. Shaffer questioned the language “clinically important differences” and asks if there is a reason to include “clinically”? He raised the need to identify whether statistical differences are clinically significant and not sure it can be specified by a review of the literature as to whether something is clinically important or not. Dr. Goldberg stated that he recalled the

subcommittees had struggled with the “clinically significant” language and the reason it has been included is to give them permission to have them struggle with it, because if they don’t they may not. He stated that as group clinicians, lay people and experts struggle with it and have come back to the Commission and we want them to do that. Dr. Yerby stated that he agreed the language can be ambiguous but all too often I have seen people focus on differences in laboratory values and not in patient’s function. He stated for all the difficulties we would like to make sure that the differences are differences that affect the function of people and although that is often messy by having it in here it may keep us refocusing on how people live. Dr. Shaffer stated that it doesn’t necessarily affect the review that the EPC does to have that in there or not, it just gets at that information. Dr. Weaver stated that it is mostly for the participating organizations to focus on clinical outcomes whether it be for efficacy or safety. At least to prioritize those to a higher degree. Kim Peterson stated that the EPC planned to increase the clarity of the question to specify that it is not to include an analysis of evidence for dental pain and surgical pain. She stated that the EPC was interested if clinicians wanted to include menstrual pain? Dr. Weaver stated that it was pain that the drugs were used for. Dr. Shaffer agreed and some of the anti-inflammatories are marketed more for that than others and so it is good to have evidence on that. There was discussion about where to add this to the KQ document. Dr. Yerby suggested that it fits under soft tissue pain under Populations. There was agreement to have an understanding that menopausal pain would be covered under soft-tissue pain in Populations.

[B-117] Dr. Weaver asked Kim Peterson why the EPC added dosages to the list of drugs as this was not done in previous KQ documents? Kim Peterson stated that Dr. Helfand added those and she did not know why. **Action: Dr. Weaver will raise that question at the 9/2/04 Center phone conference.**

[B-166] Dr. Weaver introduced the Key Question document for Urinary Incontinence. She stated that these also had been sent to the UI Subcommittee and there were no responses received. It was raised at the Update meeting that there was a new oral urinary incontinence drug called Sanctura released May 24<sup>th</sup>. She stated it was trospium chloride (Sanctura). Dr. Weaver stated that she asked the EPC if this would be a category 3 review, which means the original subcommittee would be reconvened and Dr. McDonagh stated if the articles fulfill the criteria than yes it would. Dr. Yerby questioned whether only the compounds listed on the document would be included in the review? Dr. Yerby stated that neurologists have been using amitriptyline for urinary incontinence forever for its anticholinergic affects, its cheap and it works for both adults and children. Dr. Weaver clarified that they use the side effect of the drug to treat urinary incontinence which was an off label use. Dr. MacKay stated that there would probably be very little literature because it is a generic drug. Dr. Yerby discusses the importance of reviewing off-label use of medications, as it is a common practice. Dr. Weaver discusses how Oregon’s SB819 prohibits the review of mental health drugs. She states that in the review of skeletal muscle relaxants review, the drugs were compared to valium as a comparator rather than as a drug being evaluated. Kathy Ketchum stated that she agrees it is a logical inclusion but there is a limitation with SB 819 and doesn’t think there is any comparative literature, e.g. comparing oxybutinin to amitriptyline because amitriptyline hasn’t been studied for this indication. Dr. Weaver talked about the off label use of gabapentin for pain and non-seizure indications and happens to be one that Oregon isn’t doing but the EPC is looking at off-label use specifically for the anti-convulsants. Dr. Shaffer stated there would be literature for imipramine which is used in children but that won’t be directly compared to those used for adult patients and in fact is in the Inclusion Criteria. Dr. Yerby said it would be interesting to see if there is some use of it in elderly patients with incontinence because these drugs would be found in both extremes of life for the same problem so there may be a very small literature for its use

there as well and probably won't see much of a comparison. Dr. Weaver asked if there was any interest in broadening it to include children? Dr. Yerby stated that if it did include children you might find some comparative studies because incontinence is a very common problem and how can you get approval for a drug for incontinence in children without some sort of comparison to some gold standard. Dr. Weaver stated the FDA requirement is that it has to be greater than placebo, there may not be head to head trials but she can bring it up. Dr. Shaffer stated the way it may be of interest is that these medications are starting to be used for childhood enuresis too and whether there is some literature to document that would be of interest and questioned whether it would be of interest to OMAP. Kathy Ketchum stated it would be of interest. Paul Tiffany questioned if including children would require reconvening the subcommittee? Dr. Weaver stated it wouldn't require reconvening but she would inform them of the recommendation and since there is a new drug the subcommittee will probably be reconvened for that and can look at this also. Dr. Shaffer stated that this review was for urinary incontinence in adults, which is mostly elderly, and that is a separate clinical topic than enuresis. **Action: Dr. Weaver will get feedback from the UI Subcommittee about including children when it convenes for the next review. Dr. Weaver will also recommend adding the drug, Sanctura, possibly include tricyclics and consider broadening the review to include children, or a separate review for children, at the 9/2/04 Center phone conference.**

[B-389] Dr. Weaver introduced the Skeletal Muscle Relaxant draft Key Question document and stated there was no feedback from the subcommittee. It was brought up at the Standing Update Committee meeting that under Interventions all the benzodiazepines should be listed. She stated that this would have to be an indirect comparison as these are precluded by SB819 from being reviewed. A question was raised why gabapentin was removed. Kim Peterson stated that they were added inadvertently and gabapentin is covered in controlled head to head studies and the EPC doesn't search for them specifically but they do come up in the review of the literature so they didn't need to be listed separately. Dr. Yerby asked that gabapentin be left in and that it is an off label use for spasticity. Kathy Ketchum stated that being taken off the Key Question document doesn't affect availability, as it is a drug that is covered. **Action: Dr. Weaver will recommend that gabapentin be left in the KQ document during the 9/2/04 Center phone conference.**

[B-498] Dr. Yerby asked to re-review the Calcium Channel Blocker Key Question, as he was not present during the earlier discussion. He stated that CCBs are used to treat other conditions than hypertension and whether it was appropriate to expand those KQ to look at those other conditions? He stated from a neurological view CCBs would be used quite widely to treat vassal spasm in inercranial hemorrhage and as a prophylaxis for migraine. Dr. Weaver stated that the subcommittee focused on the cardiac indications and excluded the ophthalmologic, which they are also used to treat and this could be brought up to the subcommittee. Dr. Weaver stated that migraine was covered in the Beta Blocker review. Kim Peterson said if the Center collaboration voted to enhance the review then the EPC would consider it and review the literature as she had no idea what amount of literature there was at this point. Dr. Yerby stated the literature is not large and neurologists use CCBs more than BBs to treat these conditions but there are no head to head comparisons. Kathy Ketchum stated that migraine is a prevalent condition in the Medicaid population and would be interested to see if there are some CCBs better than others and if there is literature that could change their choices. Dr. Yerby stated that if other compounds could be identified other than triptans, which are expensive, would be a service to patients. Dr. MacKay stated that it is known that CCBs work for hypertension and so do they differ in efficacy, side effects and in subgroups. Then the

question now being raised is do they actually work in preventing migraine headaches and is there any literature that they do and is there a specific compound that shows superiority. Dr. Weaver stated that if there were a CCB that worked well for migraine prophylaxis but didn't rate as high for hypertension, at least it would be on the formulary for people who need it for that reason. **Action: Dr. Weaver will ask at the Center phone conference if the review of CCB can include treatment for migraines prophylaxis.**

[B-698] An Pham, PharmD, Reliant Pharmaceuticals, gave testimony on the CCB Key Question. Dr. Pham asked if the review could include whether there is a class effect regarding edema. Dr. Weaver stated that the EPC doesn't always list all the side effects. Kim Peterson stated that the EPC review does include a comparison regarding dihydropyridines but haven't really found anything, but it is in the report now. Dr. Weaver advised that Dr. Pham can give his feedback directly to the Center and she would give him the website address after the meeting.

[B-770] No public comment was received on the Oral Hypoglycemic, NSAIDs, or Urinary Incontinence Key Questions.

[B-778] Tom Woods, Boehringer Ingelheim testified on the Urinary Incontinence Key Question. Mr. Woods stated that there is a new medication that will be out in a few months for stress urinary incontinence called duloxetine that the commission may want to consider. He stated the studies have been out for some time and the company is planning on launching it the beginning of next year. Dr. Weaver stated that the focus has been on urge incontinence and asked if there is an overlap? Mr. Woods stated the literature talks about that and it is the first drug ever indicated for stress urinary incontinence. It is anticipated that this will be huge and would be helpful for the committee to know this is coming. Paul Tiffany stated that this addresses his concerns that the reviews may be limited because the KQ only talks about urge incontinence and suggests that "urge" should be removed from the KQ. **Action: Dr. Weaver will ask the subcommittee about whether to recommend deleting "urge" so the review will cover stress urinary incontinence also.**

[B-855] No public comment on the SMR Key Questions.

[B-899] There was discussion that none of the Key Question documents were recommended for changes but that staff will take specific questions back to the subcommittees for consideration. Dr. Shaffer stated that the commission can change the Key Questions as they are the Commission's Key Questions. Paul Tiffany stated that he was reluctant to do so without input from the people selected to put them together for the commission. Paul Tiffany reiterated the process was that Dr. Weaver will take their recommendations to the Center phone conference and they may or may not be accepted. Diane Lovell stated that it was the recommendation from the commission that CCB KQ document be modified to review treatment for migraines. Dr. Goldberg stated that if they don't the commission could have a process that would include those, sort of parallel but separate from that if the commission feels strongly about that. Diane made a motion to request Dr. Weaver to ask the DERP collaboration to include treatment of migraines in the CCB review.

[Tape 2, Side A-003] **Action: The CCB Key Questions were approved as modified. Dr. Weaver will recommend to the DERP collaboration to include the treatment of migraines in the CCB review.**

[Tape 2, Side A-013] **Action: Dr. Weaver will recommend to the DERP collaboration to remove "adult" from all Oral Hypoglycemic Key Questions and Inclusion Criteria so the**

review will cover pediatrics and include the drugs, metformin and clizone. The OH Key Question document was approved as modified.

[Tape 2, Side A-033] **Action:** Dr. Weaver will recommend to the DERP collaboration to add COX-2 Inhibitors to KQ 2 and 3 after NSAIDs (NSAIDs/COX-2 Inhibitors), include menstrual pain under soft-tissue pain, replace all references to 'coxibs' with "COX-2 Inhibitors", and include the salsalate group. Dr. Weaver will also ask why the dosages are listed and also the complex question about the combination of aspirin, NSAID/COX-2 and the cardiac GI effects. The NSAID Key Questions were accepted as modified.

[Tape 2, Side A-138] **Action:** Dr. Weaver will recommend to the DERP collaboration to add to the Intervention column of the Urinary Incontinence Key Question document the drugs imipramine and amitriptyline, and the new drug, Sanctura. The Key Questions document was approved as modified. Dr. Weaver will also talk with a pediatrician about including peds on this review. Dr. Weaver will also advise the DERP collaboration about the new drug coming for stress incontinence, Duloxetine, and whether this would be a separate review.

[Tape 2, Side A-140] **Action:** Dr. Weaver will recommend to the DERP collaboration to reinstate gabapentin and to include all the benzodiazepines in the KQ for Skeletal Muscle Relaxants. The SMR Key Question document was approved as modified.

[Tape 2, Side A-152] Dr. Weaver introduced the draft Key Question document for "Newer Antiplatelets". There was discussion about why Aggrenox was in combination with aspirin but does specify that it would be reviewed as monotherapy or in combination with aspirin. It was determined that aspirin will be the comparator with all these medications. Dr. Shaffer stated that a question they want answered clinically is there a benefit to one of the newer agents in patients who have had strokes previously while on aspirin, which will probably come out in the literature search. No public comment was given. **Action:** Dr. Weaver will recommend to the DERP collaboration to add Dipyridamole with an asterisk under Interventions. The New Antiplatelet Key Question document was approved as modified.

[Tape 2, Side A-300] Dr. Weaver introduced the Bisphosphonates Key Question document. Dr. Yerby stated that it is apparent that people treated with anti-convulsant drugs, particularly the older generation anti-convulsant drugs, after about 10 years of continuous treatment are now developing osteoporosis in both men and women, e.g. dilantin, phenobarbital, carbamazepine, and maybe add this with glucocorticoid. This would address people who have seizures, fall and fracture a hip. So, doesn't affect just older people. No public comment was given. **Action:** No changes were recommended and the Bisphosphonate Key Question document was approved.

## 6. Conflict of Interest Declarations

[Tape 2, Side A-441] Dr. Weaver thanked the commission members for completing the Conflict of Interest forms. She stated that if someone has Honorarium or whatever it would be declared and invited commission members to declare those so that it was on the record. No declarations were made. She stated there was nothing in them that precluded anyone from being on the commission. She stated they are available upon request.

[Tape 2, Side A-463] Paul Tiffany stated that he will not be at the next meeting and asked that Diane not be replaced by then. Dr. Weaver stated she appreciated all the input the time they took to discuss the Key Questions and feels much better about going to this conference call

having the input from a lot of different people with different perspectives and adds to the whole project.

**Meeting adjourned.**

Handouts:

- a) 8-20-04 Agenda
- b) 7-16-04 Minutes
- c) CCB Update #1 Report
- d) New Subcommittee Roster
- e) Draft KQ for CCB Update #2
- f) Draft KQ for OH Update #2
- g) Draft KQ for NSAID Update #3
- h) Draft KQ for UI Update #2
- i) Draft KQ for SMR Update #2
- j) Draft KQ for Antiplatelets
- k) Draft KQ for Bisphosphonates

**MINUTES**  
**HEALTH RESOURCES COMMISSION**  
**September 17, 2004**

**Members Present/Phone:** Chair, Walter Shaffer, MD - Vice-Chair, Diane Lovell - James H. MacKay, MD - Dean Haxby, PharmD - Steve DeLashmutt, MD

**Members Absent:** - Dan Kennedy, RPh - Paul Tiffany - Mark Yerby, MD

**Staff Present:** Kathleen Weaver, MD, HRC Director – Betty Wilton, HRC Project Coordinator

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**1. Call to Order and Roll Call**

[A-001] Meeting was called to order by Chair, Walter Shaffer, MD and roll call taken. While waiting for Dr. Haxby, the meeting was convened with no decisions being made.

**2. Approval of Minutes**

[A-020] **Action:** The 7-16-04 Minutes were unanimously approved when Dr. Haxby joined the meeting.

**3. AARP Update**

[A-022] Jerry Cohen, State Director for AARP, Oregon State Office. Jerry explained that the name is now changed to AAP because it is not for retired persons only. Jerry stated he was presenting on behalf of the National AARP and how proud the National organization is of the work this commission and Oregon has done in the area of evidence-based practice of medicine in general and of the evidence-based research on prescription medication in particular. Jerry stated that 33 AARP state sites now link to the Oregon research on the AARP national website. He stated that the Medicare Bill of 2003 did include a section aggressively supported by AARP for funding and recognition of further funding for evidence-based practice and medicine. The Center for Medicare/Medicaid Services apparently as it continues to deal with education and ease on enrollment for the Medicare prescription drug transition card program now has, without referring to evidence-based practice, a section that allows folks to look at and print off and talk to their physicians about drugs that may be cheaper but perhaps as equally effective for them. He notes that all this started here (at HRC). He stated that AARP has now created a watchdog section on their website that looks at the industry and practices as far as cost and practices around prescriptions. Jerry handed out a sheet that highlights from Jan to August what AARP is working on promoting the outstanding work of this commission and the State of Oregon. There is currently an AARP Oregon Rx website that puts into consumer-friendly language including tables, information for consumers.

[A-069] Jerry gave a second handout that outlined the number of hits on the site, which is substantial. Dr. MacKay asked what percentage of people over 65 are able to get on the web? Jerry stated the best information that he had seen recently in Oregon is 67% of people over 50. Jerry stated that the numbers in the Pacific NW are much higher than the national average. He stated they work with the Libraries and Senior Centers to get info out to seniors of alternative ways of getting to the web.

[A0111] Jerry stated that the next addition to the web page is implementing a nationwide web page that would look at the EPC reports rather than the HRC reports.

[A120] Jerry stated that they in teamwork with the OMA, OSPA, ACPOr are two brochures he handed out. "Read, Compare, Ask" is the same mantra they are using. There is also a palm card he handed out. 55,000 brochures were sent out through the OSPA to large pharmacies and they are working on a plan to put brochures out through ACP and the OMA. He stated they are also doing community forums to primarily create a baseline of information of what we might want to update on these brochures and to ultimately create a video. He stated that Dr. Labby, Dr. Weaver, Dr. Baumeister and Dan Kennedy have been helping with the community forums.

[A-180] Jerry played a video of television infomercials that is playing currently on several channels. They are also looking at a newsprint insert that highlights for Oregonians that would go to about a million households. They also are promoting enrollment in the Oregon Prescription Drug Program (OPDP), which uses the evidence-based practice research as a tool in trying to negotiate discounts for prescription drugs and so the larger the body of people enrolled in the program, the more leverage for negotiating discounts.

[A-216] Dr. Weaver explained that SB875 and the OPDP went through the last legislature to create a purchasing group for low income Oregonians but would also eventually include perhaps PEBB, the prisons, the OHSU, etc. Missy Dolan is getting this program set up and is in the process of doing RFPs for PBMs. It is currently focused on seniors and the drugs they use the most help. Eventually, it may tie in with other states that are doing the same thing.

[A-236] Jerry stated the national AARP agenda for affordability includes looking at taking best-practice medicine applying it in ways the include purchase pooling, multi-state and also looking at better marketplace practices in terms of transparency of the system itself.

**Action: Dr. Weaver will ask Missy Dolan to give a report to the HRC.**

[A-260] Jerry stated that they are also piloting an outreach program with some volunteers that want to go visit clinics, doctors offices and pharmacies to help follow-up on distribution materials at site and we're piloting to make sure we are not stepping on anyone's toes or anything else but we see this as one more way to engage some of our members in ways to make a difference and also let the medical community healthcare professionals know "thank you" we care, and we appreciate your helping promote this information and evidence-based practice. They also hope to create a brief video news release because they have learned that when they say evidence-based practice of any sort the average citizen in the newsrooms don't seem to know how to play that story and so they are working on something to make that easier to present. They also plan to take the feedback they have received in the community forums into a very short video piece that can be used in presentations for various public audiences. They are looking for personal stories from people who have used the reports and saved money. Dr. Weaver relayed feedback from a presentation she gave recently where a woman asked why she had to pay a \$50 copay for VIOXX? She explained to her how to look up the information on the website and to talk to her doctor.

[A-326] Dr. Weaver referred to the statistics of the hits on the website, it amounts to about a half million people per year that access the reports which indicates the information is being disseminated.

[A-339] Jerry stated that they are trying to emphasize the relationship between doctor and patient and to keep the message simple by letting people to make it clear that they are having difficulty paying for the medication. He also stated they are promoting the transition card for a \$600 credit. They are working with the States Senior Health Insurance Benefits Assistance program (SHIBA). They are working with volunteers to disseminate information on the evidence-based process.

[A365] video played.

Jerry explained the different handouts he had, i.e. CD of video from last September, VHS version and various brochures discussed earlier.

[A-432] Dr. Shaffer commended AARP for all the work they are doing disseminating the evidence-based information that the HRC has been collecting. Jerry also mentioned that Paul Tiffany was one of the volunteers from AARP who worked in promoting enactment of legislation and appreciate that he is continuing the work by serving on the Commission. He also mentioned that they would appreciate getting stories of people who have benefited from this work.

[A-466] Dr. Weaver talked about an article in Health Affairs about direct-to-consumer advertising where they tried to put simple evidence-based research be part of the advertisement. She mentioned the OMA and AMA putting pressure on the FDA to require that. **Action: Dr. Weaver will bring the article to the next meeting.**

[A-486] Jerry talked about AARP having a representative on the Governor's Prescription Roundtable and they have developed a "toolkit" that is meant for employers regarding prescription drug cost and also includes a section on evidence-based practice and research. Diane Lovell stated that the employer was taken out so the toolkit could be utilized by any group. Diane also stated that Regence is developing a website that compares costs by entering a drug and brings up the costs at various pharmacies within your community and will be accessed by the public.

#### **4. OMAP Update**

[A-518] Allison Knight, Assistant Manager, OMAP, gave an update. She stated they are preparing for the next legislative session and the state is facing another huge budget deficit of around half a billion dollars and so the Oregon Health Plan will probably be impacted severely. She stated they are looking different scenarios on how to restructure benefit packages and who to cover, etc. The other thing they are looking at the impact of the MMA and Medicare changes in 2006. She stated it is a huge change for Medicaid programs. They currently have about 50,000 people on Medicaid that will be impacted that are dually eligible and over half are in long-term care. They have been reviewing the regulations that have come out, getting ready to submit formal comments, which ends October 4<sup>th</sup>. They are heavily participating in the federal level discussions they are holding in the states. She stated that these prescription drug plans can have very restrictive formularies and they are looking for ways to soften the transition for Oregon's population onto those formularies in January 2006.

[A-567] Dr. Weaver stated she was also working on that committee along with Kathy Ketchum and Tina Kitchen and some of the big concerns for the 50,000 is the fact that they are on multiple drugs and may have been on these for a long time, they are used to getting them all through one pharmacy and they will have a 4 to 6 week transition where they have to see their physician, get their drugs changed, which is going to be one of the problems. Another problem is whether they are going to be able to continue with the medications they are on because they only are required to have two drugs in each category or one drug in each small subcategory and depends on the PBM for which drugs are going to be chosen. The third issue is that people are going to be on all different kinds of plans and the physician won't know which one they are on and which drug they can have. It will be a nightmare for the physicians. She suggested that it would help if there some way electronically to have decision support so the physician would at least know what drugs were acceptable. She stated there is also the issue of whether a patient should switch drugs such as anti-seizure medicines, cancer chemotherapy drugs, etc. Dr. Shaffer stated that the decisions will be made by the ensurers and pharmacy benefit managers and not by evidence-based review of the drug categories. Dr. Weaver suggested they look at the evidence-based reviews done so far.

[A-640] **Action: Minutes were approved by unanimous vote.**

## **5. Report from Standing Update Committee**

[A-659] Dr. Weaver stated that Dr. Labby was not available to present the Estrogen update report. Dr. Weaver went through the report and talked briefly about the new information. It was noted that the entire report was not there and some pages were missing. However, no changes were made to any of the consensus statements or the conclusion.

No public testimony was given on the Estrogen report.

**Action: The Estrogen Report was unanimously approved.**

[A-784] Dr. Weaver initiated discussion of the Key Questions for the next update. She stated that Dr. Ken Burry came to the Update Committee meeting who is an expert OB-GYN from OHSU. She referred them to a handout that outlined the recommended changes. The changes are highlighted and included differentiating between premature menopause and surgical menopause; remove “depression” and insert “dementia”. Diane Lovell asked if it was dementia induced by menopause or dementia in general. Dr. Weaver stated it was dementia in general but may need further clarification. Dr. MacKay stated it should be a separate question whether estrogens prevent dementia and that there are no studies currently. Dr. MacKay suggested leaving out the premature and surgical definitions.

[B-001] Susan Carson stated that putting surgical or natural menopause may get the distinction they are looking for.

**Action: Dr. Weaver will work more on how to craft the questions and will bring this back to the HRC if time allows.**

## **6. Subcommittee Roster**

[B-018] Dr. Weaver referred them to the Roster handout. She asked for approval of all those highlighted. She stated that upon approval by HRC she would orient new members. Whereas, in the past the orientation was done before they were approved by HRC.

**Action: The roster was approved by unanimous vote.**

## **7. Drug Class Updates**

[B-038] Dr. Weaver stated the Antiplatelet Subcommittee will have their orientation meeting and review the Key Questions in the next few weeks. The Inhaled Corticosteroid Subcommittee has been through orientation and is awaiting the EPC report. She stated that the Alzheimer Subcommittee has been through orientation also.

## **8. Key Questions for ACE Inhibitor Update #2**

[B-048] Dr. Weaver stated that the subcommittee recommended no changes to the Key Questions for the next update. Dr. Weaver stated that the public can now give direct feedback to the Center through their website.

No public testimony was given for the ACE Key Questions.

**Action: The ACE Key Questions Update #2 was unanimously approved.**

## **9. Key Questions for Statin Update #3**

[B-100] Dr. Weaver stated that the Statin Update Committee had recommended a change by adding the question at what point can you look at LDLs as a marker for cardiac disease for its lowering capabilities. She stated the Commission discussion at that time was “no” because the focus was on clinical outcomes. Dr. Weaver stated there are six statins in the US and five have clinical outcome data. Rosuvastatin does not, as it is the newest statin; however, there are articles to show that it actually gets people to goal faster than other statins. There was discussion to include rosuvastatin for a possible class effect in that if you lower LDL eventually you will show the lowering of cardiac risk and outcomes. Another issue raised was why adult

was defined as “20” instead of “18”. The recommendation from the Update Committee was to change that to “≥18”. Susan Carson, EPC, commented that 18 made more sense.

[B-167] Dr. MacKay would like to add under subgroups: diabetics because the literature is very powerful showing using them in that group vs. an 18 year old with a little high cholesterol, i.e. a very low risk person vs. a very high risk person and all the gradations in-between. So, include various subgroups based on risk factors. Dr. MacKay cautioned that maybe the drugs are being overused and the risks of side effects may be overwhelming compared to what benefit they are getting. Dr. Weaver commented on the importance of separating out the people that need to be treated aggressively with primary prevention. Dr. Shaffer stated that was the purpose of the National Cholesterol Education panel goals. Dr. Weaver suggested doing physician education about how to separate out and who to treat and not to treat before the next update. Dr. MacKay stated that once they stop taking the statin the process stops and all the years of taking it have been wasted. Dr. MacKay stated he hoped that somewhere it would address at what risk level do you start treatment? He stated, “When you take diabetics out, it is hard to show that statins do much good at all”.

[B-268] Henry Tang, R.Ph., AstraZeneca gave public testimony. Mr. Tang stated he was a cardiovascular medical information scientist with AZ, the maker of rosuvastatin (Crestor). Mr. Tang commented that in regard to whether a new agent with no clinical outcomes should be included, when you look at the LDL reduction data that was plotted vs. cardiovascular events shows that clearly with every milligram of LDL reduction there is a significant benefit and the lower is better. He read a quote from the updated ATP3 Guideline published a couple months ago “Limitations in the efficacy of LDL lowering therapy in spite of growing evidence will benefit in reducing LDL-c level to less than 70 milligrams with very high risk patients. Many such patients may not be able to achieve such low levels with current available drugs.” He stated, using minimal drug therapy just to produce a small LDL reduction that will barely attain the LDL-c goal would not be a prudent use of LDL lowering drugs”. He stated that many patients would not be able to get down to goal whether it is 100 or 70, but a more efficacious statin is needed which would eventually reduce cardiovascular outcomes. Dr. Shaffer asked if Mr. Tang had any comments on the Key Questions? Mr. Tang stated that the #3 question was deleted and he wanted to reiterate that LDL reduction and goal attainment is very critical.

**[B-318] Action: The Statin Key Question Update #3 was adopted with the modification of changing the age of adult to “≥18.**

## **10. New Projects for HRC**

[B-332] Dr. Shaffer asked for ideas and suggestions on other projects the HRC may want to review. Dr. MacKay suggested injectables. There was discussion about the different ways of reviewing injectables. Dr. Weaver stated she was attending the NW Medical Directors meeting in Washington and they are focusing on injectable drugs and will find out what they are doing in the State of Washington. Kathy Ketchum suggested bio-technology. It was suggested looking at mental health drugs as the reports are already being done by the EPC but would probably require legislation. Diane Lovell suggests moving back to technology in general especially around imaging which is where the HRC started. Dr. Weaver suggested therapies, new vs. older procedures. Dr. Weaver suggested bringing Dan Harris’ approach toward technology reviews to the next meeting as he had nice guidelines on how to do this and copies of the reports done by the HRC back then such as on Ventricular Assists or Bone Marrow Transplant for Stage 4 Breast Cancer. Dr Weaver stated there is more literature now on procedures than before. She also suggested reviewing randomized controlled studies of things that haven’t been done before, e.g. knee arthroscopy vs. a sham procedure. Dr. MacKay suggested a study on back fusions. Diane Lovell suggested the study of bariatric surgery.

[B-460] Dr. Shaffer asked what the process would be once the HRC came up with areas to study? Diane Lovell stated the process was to cast a very broad net, they asked physician groups, leadership groups, health plans, public, technology manufacturers, the state. Dr. Weaver stated she would look into the funding aspect of doing additional reviews.

[B-553] Dr. DeLashmutt stated it would be good to look at congestive heart failure technology as he read recently in the OHSU news about putting in assistive devices at the medical school now and how if everybody who needed one got an assistive device it would bankrupt the system. He asked who would listen to the evidence in setting policy? Dr. MacKay stated that Providence does technology assessment and there are some national organizations, ECRI and Hayes that do technology assessment and those assessments can be purchased at a minimal cost. Dr. Weaver suggested also maybe looking at chronic disease management.

[B-788] Dr. DeLashmutt suggested collaboration with other commissions, e.g. the Patient Safety Commission. They are working on improving patient safety, which includes technology that goes astray like IV pumps.

**Action:** Dr. Weaver will do more research and bring back more information to the next meeting. The areas suggested so far are: injectables, mental health drugs, diagnostic imaging, therapeutic, geriatric surgery, genetic testing, and chronic disease management. She will also bring back the list of what the OHP Medical Directors put together. She will also bring back some of the prior HRC history and samples of reports done previously. She will also check with the Patient Safety Commission.

**Meeting adjourned.**

Handouts:

- a) 8-20-04 Agenda
- b) 7-16-04 Minutes
- c) Estrogen Update #2 Report
- d) ALZ, ICS & AP Subcommittee Roster
- e) Draft KQ for ACE Update #2
- f) Draft KQ for STATIN Update #3

**MINUTES**  
**HEALTH RESOURCES COMMISSION**  
**November 19, 2004**

**Members Present/Phone:** Chair, Walter Shaffer, MD - James H. Mackay, MD - Dean Haxby, PharmD - Steve DeLashmutt, MD – Dan Kennedy, RPh – Paul Tiffany – Mark Yerby MD – Lynn-Marie Crider

**Members Absent:** - None

**Staff Present:** Kathleen Weaver, MD, HRC Director – Bruce Goldberg, MD, OHPR Administrator - Betty Wilton, HRC Project Coordinator

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**1. Call to Order and Roll Call**

[A-001] Meeting was called to order by Chair, Walter Shaffer, MD and roll call taken. Lynn-Marie Crider was introduced as a new Commissioner. Elaine Dunda and Diane Lovell's terms have ended, recognition plaques are to be given.

**2. Approval of Minutes**

[A-069] **Action:** The 9-17-04 Minutes were unanimously approved.

**3. DERP Governance Conference Update**

[A-074] Dr. Shaffer gave an update from the Drug Effectiveness Review Project (DERP). There are 14 participating organizations in the project of which 12 are states. They are Alaska, Arkansas, Idaho, Kansas, Michigan, Minnesota, Missouri, North Carolina, Oregon, Washington, Wisconsin, and Wyoming. Other organizations that are not states are California Healthcare Foundation and Canadian Office of Health Technology Assessment. All states and organizations are currently using the evidence-based reviews of medications and making recommendations to the Medicaid systems in each state. These preferred drug lists are having positive effects on expenditures from pharmaceutical budgets. The Commonwealth Fund will be studying effectiveness of the process. The future therapeutic groups were selected for study and they are Tissue Necrosis Factor Inhibitors (arthritis), Thioglidazones ( TZDs - oral hypoglycemic agents) and Anti-Nausea medications (5HT3).

**Action:** The three selected groups of medicines were adopted and approved.

**4. OMAP Update**

[A-515] Allison Knight, Assistant Manager, OMAP, gave an update. OMAP has finalized the supplemental rebate policies. The purpose of the supplemental rebate is to meet benchmark prices. OMAP has received a supplemental rebate offer. Effective December 1, 2004 OMAP will be adding a drug back in the class that was taken off in August because it didn't meet the benchmark price. The manufacturer of the drug offered a supplemental rebate. The OMAP cabinet made a decision that the income levels for the standard program will not be reduced.

## **5. Oregon Prescription Drug Program**

[A-704] Missy Dolan, Administrator of the Oregon Prescription Drug Program, gave an update. She gave background on the formation of the drug program. Since April, she has written and filed administrative rules talked to stakeholders and defined the operational requirements of the program. The stakeholders included members of the legislature, the pharmaceutical association, the pharmacy association, AARP, Metropolitan Alliance for the Common Good, and Oregonians for Health Security. The senate bill was very specific about who could participate. Eligible individuals include those who are residents of the State of Oregon who are at least 54 – 64 years old, have not had health insurance for six months and who are at 185% of FPL or less. Government agencies include PEBB, local government state agencies, school districts, participants in the current senior RX program, OHSU, and any government agency unless sponsored by Medicaid. A pharmacy and therapeutics committee is being formed. There is a lot of interest in expansion of this program. There is room to expand in the near-elderly population and in small businesses. AARP designed a brochure for this program. This brochure was mailed to over 200,000 Oregonians. AARP received responses from almost 10,000 individuals who are interested in saving but are not eligible to join the program. Enrollment applications will be mailed December 8, 2004 to all individuals who responded. As soon as the contract is signed with PBM, the program will go live. The program is currently in negotiation with an apparent successful bidder. Currently two drug lists will be used to start the program.

[B-005] The discounted pharmacy cost comes from the actual pharmacy and not PBM or bulk purchasing. The prescription drug program has asked in the RFP for full transparency and is negotiating for a cost-plus program. The program is trying to negotiate an administrative reimbursement for the services through the PBM. One of the requirements of the bill is that a PBM does not negotiate price with local pharmacies, the state does. The state will negotiate what is an acceptable discount.

## **6. Report from AIIRA Subcommittee**

[B-114] Dr. Rich Clark, Subcommittee Chair, gave an update. The table on page 6 of the report was reviewed. Reviewed key questions. The subcommittee's opinions to each key question were reviewed (see handout). The question was raised regarding the subcommittee's goals on efficacy in regards to cardiovascular mortality and cardiovascular events as opposed to primarily trying to lower systolic, diastolic and hypertension itself. Was the issue of lowering hypertension looked at? The Subcommittee looked at morbidity and mortality as opposed to just the blood pressure. The Key Question stated, "Is one AIIRA better than another?" There is none better than another in terms of cardiovascular outcomes at the point that it was looked at, but some are more effective at lowering systolic blood pressure. It was recommended for the subcommittee to look into this issue. The question was raised about whether the subcommittee looked at issues such as tolerability, proportion of persons completing trials and adverse experiences overall as opposed to serious complications. Dr. Weaver replied to the question. The AIIRA's appear to be well tolerated and depending on the adverse effect, patient population, and agent evaluated, reports of adverse effects were similar to, increased, or decreased compared to placebo. Withdrawal rates were generally less than placebo, except for studies in patients with heart failure. Withdrawals due to adverse events were also generally less than ACEI's, especially regarding cough. Reports of angioedema are rare with the AIIRA's, but have been reported to occur in patients previously experiencing angioedema on an ACEI. The Chair agreed to receive public testimony in regards to the AIIRA's.

[B-509] Brian Lee, Medical Liaison, Sanofi-Aventis, gave public testimony. There are currently 60 million patients in the US that have hypertension. The primary use of ACEI and AIIRA's is for the treatment of hypertension. A major flaw with this report is that there are different agents within the same class that may treat hypertension better and the data to support this is available and it was not used in the document.

[B-690] Sue Miller, Novartis, gave public testimony. She suggested that this report is flawed at the core. You cannot call the report evidence based medicine review when the primary statement is superiority based solely on head-to-head trials of the agents within the class. There are differences between the agents. When the document refers to a majority of the trials looked at a placebo, it should have stated that a head-to-head trial couldn't be done with these drugs. The exception is uncomplicated hypertension. It takes more than one medication to treat these populations of patients. It would be unsafe and unwise for the commission to put forward the recommendation in the report with just the core understanding of an ARB to ARB, head-to-head trial.

[B-889] Brian Lee gave public testimony. He addressed the issue of pharmaceutical companies not being in the process of initially providing feedback for the report. Decisions are made by the commission and related committees, and no matter what the outcome of the decisions, it is always perceived with biased intentions.

[A-005] The question was raised as to whether there is any way the commission can request the evidence based center to do the courtesy of acknowledging what has been received. Dr. Weaver stated that a response is given as far as the dossier but she asked the EPC the question of when there is opportunity to comment on either the key questions or the report itself, if the people that have commented get a response.

[A-011] The EPC responded to say that they do not believe that there is any response to comments given, but all of the public comments are passed on through the center to all of the participating organizations and to the EPC that are conducting the review. They are discussed on the Governor's call among all of the organizations. The issue was addressed that a response was not given to specific public comment. There may not have been a response but that does not mean that the comments were not considered. If the comments were about a suggestion to include studies in which the only outcome was blood pressure lowering, those still would not have been included. That decision was made at the key questions stage. If we received public comments to that effect, we still would not have included those studies. But that does not mean that the feedback was not received or considered. The decision was made that those studies are excluded. Dr. Weaver stated that Mr. Lee is being heard at the level of the subcommittee and the HRC. Dr. Weaver also stated that Mr. Lee could respond directly to the Center for Evidence-based Policy.

[A-71] Steve Wright, Account Manager for Novartis Pharmaceuticals gave public testimony. He suggested that the document is supposed to be written in manner that any physician or patient should be able to look at and be able to tell what is the best evidence for the disease that a patient has or a physician may be treating. The bullet points are often times the only things in a large document that get read. Mr. Wright is asking that the committee consider putting the evidence in a box or bullet points so that it is easier to read and understand for both patients and physicians.

**Action: Motion was made to accept the report. Moved and seconded. The report is accepted.**

## **7. Report from BB Subcommittee**

[B-213] Louise Kremkau, MD, gave a report from the Beta Blockers Subcommittee. Dr. Kremkau referred the Commission members to the key questions listed on page 9 of the report. (see report) Dr. Kremkau next referred the Commission to the table on page 21 for a summary. The Committee notes the lack of appropriate head-to-head trials that limits the committee's ability to draw firm conclusions. Areas of future study have been identified. The category of "Silent Ischemia" has been eliminated since the committees last report in March because it was not a clearly defined disorder. All 15 Beta Blockers that are available for use in this country have been reviewed by the committee. Three have been added since the March report. Reviewed question 1A (see page 10 and 11). Reviewed question 1B, page 12. There was an objection to the data in superscript 23. All but Carteolol have been found effective in the treatment of Angina in short-term studies and yet we qualify with the superscript that those that have Intrinsic Sympathomimetic Activity ISA properties including three others other than Carteolol. Dr. Kremkau asked the EPC to respond to this statement. She asked the EPC what the data is because the subcommittee based their recommendations on the EPC's summary. [A-338] Dr. Weaver refers the Commission and the EPC to the EPC report on page 11. Dr. Weaver paraphrased the summary on page 11 that represents the EPC's view. Dr. Weaver suggests that the subcommittee's report state that the findings are expert opinions and not data. The Commission would like to see opinion should be labeled and placed under consensus, but not in the conclusion.

[A-467] Dr. Louise Kremkau, MD continued to review the report with the Commission. (See report for complete details.)

[A-888] Dr. Louann Horner, medical scientist with Glaxco Smith-Klein, gave public testimony. Dr. Horner stated that she wanted to discuss issues related to Carvedilol. In patients with mild to moderate heart failure, all three drugs, Bisoprolol, Cardedilol, and Metoprolol succinate (ER), reduce mortality. That relative risk in the US over 1000 patients is 1.5. There was no mortality benefit and the FDA did not grant them a mortality phrase in the FDA indications. They also restricted that drug to efficacy in mild to moderate HF, knowing that severe HF studied, but they did not have adequate evidence from the single studies supporting the Metropolol succinate form of that drug. Dr. Horner stated that the EPC reported that Coreig has the most straight forward direct evidence. Dr. Horner stated that they are in support of the review.

[B-001] Dr. Weaver stated that the Commission and the subcommittee will continue to look at the data for all listed drugs. In superscript 23, the Commission suggests leaving the statement as is but refer to the Beta Blocker EPC report as to the specific page for that information and remove it from the conclusion on page 22. Nadolol is taken out of point number 7 in the conclusion.

**Action: Motion was made to accept the report. Moved and seconded. The report is accepted with one objection by Dr. Mark Yerby.**

## **8. Drug Class Updates**

[B-090] Dr. Weaver gave an update on the estrogen corporation's key questions. The key questions were modified according to the subcommittee suggestions. The primary information that was changed in the report is under "population." It refers to possible data to be considered separately for women with natural versus surgical menopause. Every thing else remains the same as the last Estrogen report.

**Action: Motion was made to accept the key questions as modified. Moved and seconded. The key questions are accepted as modified.**

## **9. New Projects**

[B-113] Dr Weaver stated that there will be no new reports or updated reports for December due to the holidays. There will be no meeting in December. Dr. Weaver suggested that the new project discussion be held over until January.

### **Meeting adjourned**

#### Handouts:

- a) 11-19-04 Agenda
- b) 9-17-04 Minutes
- c) Angiotensin II Receptor Antagonists Report
- d) Draft KQ for Estrogen Preparations Update #3
- e) Beta Adrenergic Blockers Report