HB 319

<TARGET><BILL>HB 319</BILL><SUBJECT>HB 319</SUBJECT><COMM>HHSS28</COMM></TARGET>

Alaska State Legislature
House of Representatives
Representative Tammie Wilson

Interim
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HB 319

Version 28-LS0199\N

Sponsor Statement

Currently wholesale companies of drugs and medical devices that are outside the state of Alaska are not required to be licensed with the State creating an unfair disadvantage to our local businesses. This bill will level the playing field by requiring these out of state wholesalers to be licensed as those are in the state. Additionally, with the potential for the counter fitting of products by rogue companies, this legislation will help insure Alaskans receive quality products.

It also adds verbiage which would include "pharmacy or pharmacist" as a "provider" under section 6 (d) which defines those occupations in which unfair discrimination is prohibited against a person who provides a service within the scope of the providers occupational license.
This bill would also require the State of Alaska to pay for and/or reimburse compounded prescription within the same scope and manner as manufactured prescriptions.
Pharmacy compounding is the creation of a particular pharmaceutical product to fit the unique need of a patient. To do this, compounding pharmacists combine or process appropriate ingredients using various tools. This is done for medically necessary reasons, such as to change the form of the medication from a solid pill to a liquid, to avoid a non-essential ingredient that the patient is allergic to, or to obtain the exact dose(s) needed or deemed best of particular active pharmaceutical ingredient(s).

Currently, a compound prescription that contains at least one legend (RX only) drug is generally covered by most insurance plans. However, the compounding pharmacy may only be reimbursed for the legend drug(s) in the compounded prescription, not the other ingredients used or for the time it took to make the compound. (This may mean that the pharmacy is unable to make up the medication per the designed formula and/or unable to dispense the intended product to the patient.) This will negatively impact our local businesses, in-fact it could put many out of business. Alaskans deserve to have coverage of compounded medications for potentially life-saving indications as well as for quality of life.

Many of these drugs were previously covered, now the customer must bear the cost anywhere from as little as $80.00 to as much as $800.00 depending on the compound.

Fiscal Note

State of Alaska
2014 Legislative Session

Bill Version: HB 319
Fiscal Note Number:
() Publish Date:

Identifier: HB319-DCCED-DOI-03-14-14
Title: DRUG/DEVICE DISTRIBUTORS; COMPOUNDED RX
Sponsor: T.WILSON
Requester: House Labor and Commerce

Department: Department of Commerce, Community and Economic Development
Appropriation: Insurance Operations
Allocation: Insurance Operations
OMB Component Number: 354

Expenditures/Revenues

Note: Amounts do not include inflation unless otherwise noted below. (Thousands of Dollars)

	FY2015 Appropriation Requested	Included in Governor's FY2015 Request	Out-Year Cost Estimates				
OPERATING EXPENDITURES	**FY 2015**	**FY 2015**	**FY 2016**	**FY 2017**	**FY 2018**	**FY 2019**	**FY 2020**
Personal Services							
Travel							
Services							
Commodities							
Capital Outlay							
Grants & Benefits							
Miscellaneous							
Total Operating	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Fund Source (Operating Only)							
None							
Total	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Positions							
Full-time							
Part-time							
Temporary							
Change in Revenues							

Estimated SUPPLEMENTAL (FY2014) cost: 0.0 *(separate supplemental appropriation required)*
(discuss reasons and fund source(s) in analysis section)

Estimated CAPITAL (FY2015) cost: 0.0 *(separate capital appropriation required)*
(discuss reasons and fund source(s) in analysis section)

ASSOCIATED REGULATIONS

Does the bill direct, or will the bill result in, regulation changes adopted by your agency? No
If yes, by what date are the regulations to be adopted, amended or repealed? n/a

Why this fiscal note differs from previous version:

Not applicable, initial version.

Prepared By: Lori Wing-Heier, Division Director — Phone: (907)465-2515
Division: Division of Insurance — Date: 03/14/2014 11:50 AM
Approved By: Jeanne Mungle, Director — Date: 03/14/14
Agency: Administrative Services

FISCAL NOTE ANALYSIS

STATE OF ALASKA **BILL NO.** HB319
2014 LEGISLATIVE SESSION

Analysis

HB319 would amend AS 21.36.090(d) to add "pharmacy or pharmacist" to the definition of the term "provider."

HB319 would also amend AS 21.55.110 to add "compounded prescriptions, regardless of whether the compounded prescription contains a legend drug" to the list of minimum benefits provided under health plans offered by the Alaska Comprehensive Health Insurance Association.

The Division of Insurance does not anticipate a fiscal impact from this legislation.

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House Bill 319

Sectional Analysis

Version 28-LS0199\N

An Act relating to wholesale drug or device distributors; relating to prescription benefits under the state health insurance plan...

Section 1: (7) Adds "or device" which would prohibit wholesale device distributors from dispensing or distributing directly to a patient.

Section 2: Adds a new section (Sec. 08.80.459) which would require out-of-state wholesale distributors of drugs or devices to be licensed with the Board and defines the manner in which the Board can regulate them.

Section 3: Adds "or device" and "or devices" which effectively defines a wholesale distributor of devices.

Section 4: Adds "or device" and "or registered" under subsection (B)(iii) as an exclusion of subsection (a).

Section 5: Adds "or device" and "or registered" under subsection (B)(ii) to the list which this section is excluded.

Section 6: Adds "pharmacy, or pharmacist" to be included in the list of professionals that may not be discriminated against under this section.

Section 7: Under (13) the verbiage "cost-effective" was cleaned up.
A new subsection was added, line (22) which would require the State to pay for compounded prescriptions whether or not they contain a legend drug, under the State's current health insurance plan, as previously covered.

Do Compounded Medications Require FDA Approval?

The FDA approval process is intended for mass-produced drugs made by manufacturers. Because compounded medications are personalized for individual patients, it is not possible for each formulation to go through the FDA's drug approval process, which takes years to complete and is prohibitively expensive, often costing hundreds of millions of dollars.

About PCCA

PCCA is an independent compounding pharmacy's complete resource for fine chemicals, devices, equipment, training & support.

What is Compounding?

Compounding is the Art and Science of Creating Personalized Medications

Pharmacy compounding is the art and science of preparing personalized medications for patients. Compounded medications are "made from scratch" – individual ingredients are mixed together in the exact strength and dosage form required by the patient. This method allows the compounding pharmacist to work with the patient and the prescriber to customize a medication to meet the patient's specific needs.

Find out more about compounded medications:

- Specialty Compounding: Compounding is a useful tool in varied areas of medicine
- Alternative Medication Forms: Making medications more effective and easier to take
- Compounding Answers: Answers to common compounding questions

A Brief History of Compounding

At one time, nearly all prescriptions were compounded. With the advent of mass drug manufacturing in the 1950s and '60s, compounding rapidly declined. The pharmacist's role as a preparer of medications quickly changed to that of a dispenser of manufactured dosage forms, and most pharmacists no longer were trained to compound medications. However, the "one-size-fits-all" nature of many mass-produced medications meant that some patients' needs were not being met.

Innovative Compounding Technology & Techniques Meet Patient Needs

Fortunately, compounding has experienced a resurgence as modern technology and innovative techniques and research have allowed more pharmacists to customize medications to meet specific patient needs.

Trained, PCCA member pharmacists can now personalize medicine for patients who need specific:

- Strengths
- Dosage forms
- Flavors
- Ingredients excluded from medications due to allergies or other sensitivities

General Requirements.

(a) Each pharmacy is of sufficient size to allow for the safe and proper storage of prescription drugs and for the safe and proper compounding and/or preparation of prescription drug orders.

(b) There is a minimum of three linear feet by a minimum of 18 inches in depth of counter working space for each pharmacist or intern compounding or filling prescriptions at the same time.

(c) The prescription department and all areas where drugs are stored are well lighted, well ventilated, dry, and maintained in a clean and orderly condition. Walls, floors, ceilings, and windows are clean and in general good repair and order.

(d) Each pharmacy has a sink with hot and cold running water within the pharmacy and maintained in a sanitary condition.

(e) There are refrigeration facilities with a thermometer in the prescription department for the proper storage of drugs requiring refrigeration. Temperatures in the refrigerator are maintained within United States Pharmacopeia standards.

(f) The temperature of the pharmacy is maintained within a range compatible with the proper storage of drugs.

Equipment and Supplies.

(a) All pharmacies have in their possession the equipment and supplies necessary to compound, dispense, label, administer and distribute drugs and devices. The equipment is in good repair and is available in sufficient quantity to meet the needs of the practice of pharmacy conducted therein.

(b) All equipment is kept in a clean and orderly manner. Equipment used in the compounding or preparation of prescription drug orders (counting, weighing, measuring, mixing, stirring, and molding equipment) is clean and in good repair.

Library. A reference library is maintained which includes the following:

(1) A current copy of the Alaska Pharmacy Statutes and Regulations.

(2) At least one current or updated reference (hard-copy or electronic media) from each of the following categories:

(A) Patient information – examples are;

(i) USP Dispensing Information; or

(ii) Patient Drug Facts; or

(iii) reference text or information leaflets which provide patient information.

(B) General information – examples are;

(i) Facts and Comparisons; or

(ii) USP Dispensing Information, Volume I (Drug Information for the Healthcare Provider); or

(iii) Remington's Pharmaceutical Sciences.

(C) Clinical Information – examples are;

(i) AHFS Drug Information; or

(ii) Micromedex; or

(iii) Clinical Pharmacology; or

(iv) reference material pertinent to the practice setting.

(3) The telephone number of the nearest poison control center is readily available.

This pamphlet is prepared by the Alaska Board of Pharmacy to establish guidelines on facilities, reference materials, equipment, supplies and other matters. Professional conduct by a licensee includes adherence to these guidelines. See 12 AAC 52.400.

STERILE PHARMACEUTICALS
February 2008

Scope and Purpose.

The purpose of this pamphlet is to provide standards for the preparation, labeling, and distribution of sterile products by pharmacies, pursuant to or in anticipation of a prescription drug order. These standards are intended to apply to all sterile products, notwithstanding the location of the patient (eg. home, hospital, extended care facility, hospice, practitioner's office).

Definitions.

(a) "Biological Safety Cabinet" – a containment unit suitable for the preparation of low to moderate risk agents where there is a need for protection of the product, personnel and environment, according to National Sanitation Foundation (NSF) Standard 49.

(b) "Class 100 Environment" – an atmospheric environment which contains less than 100 particles 0.5 microns in diameter per cubic foot of air, according to Federal Standard 209D.

(c) "Cytotoxic" – a pharmaceutical that has the capability of killing living cells.

(d) "Parenteral" – a sterile preparation of drugs for injection through one or more layers of the skin.

(e) "Sterile Pharmaceutical" – dosage form free from living micro-organisms (aseptic).

Policy and Procedure Manual.

(a) A policy and procedure manual is prepared and maintained for the compounding, dispensing, and delivery of sterile pharmaceutical drug orders. The manual is reviewed and revised as necessary on an annual basis by the pharmacist-in-charge and is available for inspection at the pharmacy.

(b) The manual includes policies and procedures, as applicable, for:

(1) Clinical services;
(2) Sterile product handling, preparation, dating, storage and disposal;
(3) Major and minor spills of cytotoxic agents;
(4) Disposal of unused supplies and medications;
(5) Drug destruction and returns;
(6) Drug dispensing;
(7) Drug labeling;
(8) Duties and qualifications for professional and nonprofessional staff;
(9) Equipment use and maintenance;
(10) Handling of infectious waste pertaining to drug administration;
(11) Infusion devices and drug delivery systems;
(12) Training and orientation of professional and non-professional staff commensurate with the services provided;
(13) Dispensing of investigational medications;
(14) Quality control and quality assurance;
(15) Recall procedures;
(16) Infection control;
(17) Suspected contamination of sterile products;
(18) Orientation of employees to sterile technique;
(19) Sanitation;
(20) Security; and
(21) Transportation.

Physical Requirements.

(a) The pharmacy designates an area for the preparation of sterile products that is functionally separate from areas for the preparation of non-sterile products and is constructed to minimize traffic and airflow disturbances. It is used only for the preparation of these specialty products. It is of sufficient size to accommodate a laminar airflow hood and to provide for the proper storage of drugs and supplies under appropriate conditions of temperature, light, moisture, sanitation, ventilation, and security.

(b) The pharmacy preparing parenteral products has:

(1) Appropriate environmental control devices capable of maintaining at least a Class 100 environment condition in the workspace where critical objects are exposed and critical activities are performed; furthermore, these devices are capable of maintaining Class 100 environments during normal activity;

(2) When cytotoxic drug products are prepared, appropriate environmental control also includes appropriate biological safety cabinets;

(3) Sink with hot and cold running water which is convenient to the compounding area for the purpose of hand washing prior to compounding;

(4) The designated area shall have hard cleanable surfaces, walls, floors and ceilings;

(5) Appropriate disposal containers for used needles, syringes, etc. and if applicable, for cytotoxic waste from the preparation of chemotherapy agents and infectious wastes from patient's homes;

(6) Refrigerator/freezer with thermometer;

(7) Temperature controlled delivery container, if appropriate;

(8) Infusion devises, if appropriate;

(9) Supplies adequate to maintain an environment suitable for the aseptic preparation of sterile products.

(c) Laminar flow hood certification (or clean room certification, if applicable) are conducted at least every six months by an independent contractor according to Federal Standard 209B or National Sanitation Foundation 49 for operational efficiency. These reports are maintained for at least two years. In addition, prefilters are replaced on a regular basis and the replacement date documented.

(d) The pharmacy has current reference materials related to sterile products. These reference materials will contain information on stability, incompatibilities, preparation guidelines, and the handling of chemotherapy drug products.

Personnel.

(a) All personnel participating in the preparation and/or dispensing of compounded sterile pharmaceuticals are trained in this specialized function, including the principles of aseptic technique. All duties and responsibilities of personnel are consistent with their training and experience.

(b) Pharmacies providing parenteral products to non-hospitalized patients have a pharmacist accessible twenty-four hours per day to respond to patient's and other health professional's questions and needs.

Drug Distribution and Control.

(a) In addition to labeling required for all dispensed prescription drug orders, the labeled container of a sterile pharmaceutical bears the expiration date of the preparation based upon published data.

(b) Delivery Service. The pharmacist-in-charge assures the environmental control of all products shipped. Therefore, any compounded sterile pharmaceutical is shipped or delivered to a patient in appropriate temperature controlled (as defined by United States Pharmacopeia Standards) delivery containers and stored appropriately in the patient's home or outpatient location.

(c) Disposal of Infectious/Hazardous Waste. The pharmacist-in-charge is responsible for assuring there is a system for the disposal of cytotoxic waste and infectious waste in a manner so as not to endanger the public health.

(d) Emergency Kit. When sterile pharmaceuticals are provided to home care patients, the pharmacy may supply the licensed nurse with emergency drugs, if the prescribing practitioner has authorized the use of these drugs by a protocol for use in an emergency situation (e.g. anaphylactic shock).

Cytotoxic Drugs.

The following additional requirements are necessary for those pharmacies that prepare cytotoxic drugs to assure the protection of the personnel involved:

(a) All cytotoxic drugs are compounded within a vertical flow, Class II, Biological Safety Cabinet. Policy and procedures are developed for the cleaning of the laminar airflow hood between compounding cytotoxic drugs and other parenteral products, if applicable.

(b) Protective apparel is worn by personnel compounding cytotoxic drugs. This includes disposable gloves and gowns with tight cuffs.

(c) Appropriate safety and containment techniques for compounding cytotoxic drugs are used in conjunction with the aseptic techniques required for preparing sterile products.

(d) Disposal of cytotoxic waste complies with all applicable local, state, and federal requirements.

(e) Written procedures for handling both major and minor spills of cytotoxic agents are developed and included in the policy and procedure manual.

(f) Prepared doses of cytotoxic drugs are dispensed, labeled with proper precautions, and shipped in a manner to minimize the risk of accidental rupture of the primary container.

Patient Training.

If appropriate, the Pharmacist demonstrates or documents the patient's training and competency in managing the type of therapy provided by the Pharmacist to the patient in the home environment. A pharmacist is involved in the patient training process in any area that relates to drug compounding, labeling, storage, stability, or incompatibility. The Pharmacist is responsible for seeing the patient's competency in the above areas is reassessed on an ongoing basis.

Quality Control and Quality Assurance Procedures.

(a) Quality Control. There is a documented, ongoing quality control program that monitors and evaluates personnel performance, equipment and facilities. Procedures are in place to assure the pharmacy is capable of consistently preparing pharmaceuticals which are sterile and stable. Quality control procedures include, but are not limited to, the following:

(1) recall procedures;

(2) storage and dating;

(3) documentation of appropriate functioning of refrigerator, freezer, and other equipment;

(4) documentation of aseptic environmental control device certification and the regular replacement of prefilters;

(5) a process to evaluate and confirm the quality of the prepared pharmaceutical product; and

(6) if bulk compounding of parenteral solutions is performed utilizing non-sterile chemicals, extensive end product testing is documented prior to the release of the product from quarantine. This process includes appropriate tests for particulate matter and pyrogens.

(b) Quality Assurance.

(1) There is a documented, ongoing quality assurance program for monitoring and evaluating personnel performance and patient outcomes to assure efficient drug delivery, patient safety, and positive patient outcomes.

(2) There is documentation of quality assurance audits at regular, planned intervals which may include infection control, sterile technique, delivery systems/times, order transcription accuracy, drug administration systems, adverse drug reactions, and drug therapy appropriateness.

(3) A plan for corrective action of problems identified by quality assurance audits is developed which includes procedures for the documentation of identified problems and action taken.

(4) A periodic evaluation of the effectiveness of the quality assurance activities is completed and documented.

This pamphlet is prepared by the Alaska Board of Pharmacy to establish guidelines for a pharmacy or pharmacist that prepares or dispenses sterile pharmaceuticals. Professional conduct by a licensee includes adherence to these guidelines. See 12 AAC 52.430.

(a) A pharmacist may compound drugs in limited quantities before receiving a valid prescription drug order if the pharmacist has a historical basis of valid prescription drug orders generated solely within an established relationship between the pharmacist, a patient, and a prescribing practitioner for the amount of drugs compounded. Compounding drugs in an amount above that for which there is a historical basis is considered manufacturing.

(b) Compounding includes the preparation

(1) according to a prescription drug order of drugs or devices that are not commercially available;

(2) of commercially available products from bulk when the prescribing practitioner has prescribed the compounded product on a per prescription basis and the patient has been made aware that the compounded product will be prepared by the pharmacist.

(c) When a compounded product is to be substituted for a commercially available product, both the patient and the prescribing practitioner must authorize the use of the compounded product. The pharmacist shall document these authorizations on the prescription drug order or in the computerized patient medication record. The prescribing practitioner's authorization is in addition to signing to permit substitution on a prescription drug order or advising verbally that substitution is permitted. The reconstitution of commercially available products according to the manufacturer's guidelines is permissible without notice to the prescribing practitioner.

(d) A pharmacist may not offer compounded drug products to prescribing practitioners, pharmacists, or pharmacies for resale except in the course of professional practice for a prescribing practitioner to administer to an individual patient. The distribution of inordinate amounts of compounded products without a relationship between the pharmacist and the prescribing practitioner and patient is considered manufacturing.

(e) A pharmacist may receive, store, and use drug substances for compounding prescriptions that meet official compendia requirements. A pharmacist shall use the pharmacist's professional judgment to receive, store, and use drug substances for compounding prescriptions not found in official compendia.

PERSONNEL

A pharmacist engaging in compounding shall maintain proficiency through current awareness and training. Continuing education should include training in the art and science of compounding and the rules and regulations of compounding.

COMPOUNDING FACILITIES

(a) A pharmacy engaging in compounding shall have a specifically designated and adequate area for the orderly compounding of prescriptions that is maintained in a good state of repair and for the placement of materials and equipment. There is a minimum of three linear feet by a minimum of 18 inches in depth of counter working space for each pharmacist or intern compounding or filling prescriptions at the same time.

(b) Bulk medications and other chemicals or materials used in the compounding of medications must be stored in adequately labeled containers in a clean, dry, and temperature controlled area or, if required, under proper refrigeration.

(c) Adequate lighting and ventilation must be provided in all drug compounding areas. Potable water must be supplied under continuous positive pressure in a plumbing system free of defects that could contribute contamination to any compounded drug product. Adequate washing facilities, easily accessible to the compounding area of the pharmacy must be provided. The facilities must include hot and cold water, soap or detergent, and air-driers or single use towels.

(d) The area used for the compounding of drugs must be maintained in a clean and sanitary condition. It must be free of infestation by insects, rodents, and other vermin. Trash must be held and disposed of in a timely and sanitary manner. Sewage and other refuse must be disposed of in a safe and sanitary manner.

(e) If drug products with special precautions for contamination, such as penicillin, are involved in a compounding procedure, appropriate measures, including either the dedication of equipment or meticulous

cleaning of contaminated equipment prior to its use for the preparation of other drugs, must be used in order to prevent cross-contamination.

RECORDS AND REPORTS

(a) A pharmacist shall keep records of all compounded products for two years. The records must be readily available for authorized inspection at the pharmacy.

(b) A pharmacist shall ensure that there are formulas maintained electronically or manually. A formula must include ingredients, amounts, methodology and equipment, if needed, and special information regarding sterile compounding.

(c) A pharmacy engaging in compounding must have written procedures for the compounding of drugs to assure that the finished products have the identity, strength, quality, and purity they are represented to possess. The procedures must include a listing of the components, their amounts in weight or volume, the order of component mixing, and a description of the compounding process. The procedures must list all equipment and utensils and the container or closure system relevant to the sterility and stability of the intended use of the drug. The procedures must be followed in the execution of the drug compounding procedure.

(d) A pharmacist shall accurately weigh, measure, or subdivide as appropriate the components for drug product compounding. The compounding pharmacist shall check these operations at each stage of the compounding process to ensure that each weight or measure is correct as stated in the written compounding procedures. If a component is transferred from the original container to another container, the new container must be identified with the component name and the weight or measure.

(e) To assure the reasonable uniformity and integrity of compounded drug products, written procedures must be established and followed that describe the tests or examinations to be conducted on the product compounded. The control procedures must be established to monitor the output and to validate the performance of those compounding processes that include the following when appropriate:

(1) capsule weight variation;

(2) adequacy of mixing to assure uniformity and homogeneity;

(3) clarity, completeness, or pH of solutions;

(f) A pharmacy engaging in compounding shall establish and follow appropriate written procedures designed to prevent microbiological contamination of compounded drug products purporting to be sterile. The procedures must include validation of any sterilization process.

(g) For the purpose of compounding in quantities larger than required for immediate dispensing by a prescriber or for future dispensing upon prescription, a pharmacy shall maintain records that include

(1) the date of preparation;

(2) the lot numbers – the lot numbers may be the manufacturer's lot numbers or new numbers assigned by the pharmacy. If a lot number is assigned by the pharmacy, the pharmacy shall record the original manufacturer's lot numbers and expiration dates, if known. If the original manufacturer's lot numbers and expiration dates are not known, the pharmacy shall record the source and acquisition date of the components;

(3) the expiration date of the finished product. This date may not exceed 180 days or the shortest expiration date of any component in the finished product unless a longer date is supported by stability studies in the same type of packaging as furnished to the prescriber or to be stored in until dispensing. Shorter dating than set forth in this subsection may be used if it is deemed appropriate in the professional judgment of the responsible pharmacist;

(4) the signature or initials of the pharmacist performing the compounding;

(5) initials of the person preparing each process;

(6) initials of the pharmacist supervising each process;

(7) a formula for the compounded product maintained in a readily retrievable form;

(8) the name of the manufacturer of the raw materials;

(9) the quantity in units of finished products or grams of raw materials; and

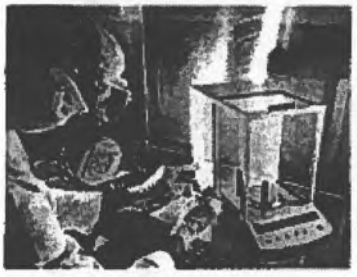
(10) the package size and the number of units prepared.

(h) "Component" means any ingredient intended for use in the compounding of a drug product, including those that may not appear in the product.

This pamphlet is prepared by the Alaska Board of Pharmacy to establish guidelines for a pharmacy or pharmacist on compounding practices. Professional conduct by a licensee includes adherence to these guidelines.
See 12 AAC 52.440.

Quality Control/Quality Assurance

Commitment to Quality



"Lives depend on a job well done." For PCCA, it's not just a saying, but the way we approach Quality. While our members have access to over 4,580 active and non-active chemicals – more than any other compounding pharmacy supplier – the competitive advantage we bring our members is the industry's most comprehensive quality control and assurance program we bring to those chemicals every day.

Here is how we differ from the competition:

Every Lot - Not Just the Initial Lot - Is Tested

- We do not solely rely upon the USP or manufacturer's label to ensure the quality of the chemicals received.
- Every lot received is tested using Fourier Transform Infrared Spectroscopy, ultraviolet-visible analysis, melting point, specific gravity, solubility and chemical identifications.
- Additional testing of APIs is done using actual formulations.

14 Checks and Analyses Are Performed on Each Chemical Lot As It Comes In and Is Repacked

- Nine qualitative and quantitative analyses are performed on every incoming chemical lot before it is released for repacking or sale.
- Each lot is tested against the certificate of analysis (C of A), including: USP, EP, NF, FCC, ACS and PCCA standards.
- After initial testing, all results are reviewed for accuracy by a second QC analyst.
- Chemicals are tested only by degreed Chemical Analysts.

Five Validation Checks Are Made During Each Repack Order, Including:

- Written and audited Label Control procedures.
- Production audits performed by the QA department followed by a second identity test performed by QC department on repacked chemicals.

PCCA Rejects About 180 Chemical Lots Per Year, or Just Over Three Lots Received Per Work Week

- PCCA is fully registered by the FDA, DEA and State of Texas as a manufacturer and follows current Good Manufacturing Practices (cGMP).
- Only FDA-registered and GMP-certified manufacturers are used for the purchase of active pharmaceutical ingredients (APIs).

Dr. Pamela Smith and Dr. John Monaco discuss the quality of PCCA bases and chemicals.

Quality Doesn't Stop With High-Quality Chemicals

Compounding pharmacies complete the quality circle by testing their compounded preparations through an independent lab such as Eagle Analytical Services. Eagle Analytical helps pharmacists close the quality circle by testing preparations on an ongoing basis including sterility testing, bacterial endotoxins, microbial detection, beyond-use date (BUD) determination and active-ingredient potency. They not only test the preparation, they test the processes behind the preparation, giving pharmacies top-to-bottom confidence in their products.

- Dedicated service, expertise, and state-of-the-art equipment.
- Timely online access to test results.
- Eagle Analytical coordinates with PCCA consultants to troubleshoot your problem compounds.

Find out more about Eagle Analytical's quality testing by visiting www.eagleanalytical.com.

Watch the video below, in which Bill Zolner, PhD, Chief Scientific Officer of Eagle Analytical Services, describes process verification.

Click here to download more information from Dr. Zolner about quality.

Click here for more information about Eagle services.

Contact PCCA

Toll-Free 800.331.2466
Local: 281.933.8845
9901 South Wilcrest Drive
Houston, TX 77099

Find a Compounder

- Answers to Your Compounding Questions
- Compounding & Patients
- Talk to Your Doctor about Compounding
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PCCA Resources

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About PCCA

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About PCCA

What is PCCA?

History

More than three decades ago, a physician encountered a patient who required an anti-nausea medication that was no longer commercially available. The physician challenged a Houston-area pharmacist to compound the medication, so the pharmacist consulted with his peers and procured the chemicals necessary to prepare it.

The prescription was a success, and the pharmacist realized that others in his field faced similar demands to help patients who require compounded medications. This network of pharmacists, united by a commitment to meet patient needs, was the foundation of PCCA (Professional Compounding Centers of America), which was incorporated in 1981.

Today, PCCA has become the independent compounding pharmacist's complete resource for fine chemicals, equipment, devices, flavors, ACPE-accredited training and education, pharmacy software, marketing, business and pharmacy consulting assistance. Our membership includes more than 3,900 independent community pharmacists in the United States, Canada, Australia, and other countries around the world.

Quality

PCCA offers unparalleled quality control and quality assurance.

PCCA's Quality Control department is exhaustively devoted to assuring the quality of the chemicals received, repackaged, and sold to our members. From the moment a chemical arrives to the time it ships to a member, it is monitored by Quality Control and Quality Assurance personnel. The dedicated QC lab performs as many as nine qualitative analyses on each chemical lot, and reviews the results and specifications of the Certificate of Analysis.

If the product is compromised in any way, it fails the inspection and is rejected. Inspection of incoming materials is paramount to the quality system and compliance with current Good Manufacturing Practices and Regulations.

Steps include:

- Obtaining a Certificate of Analysis for all chemicals received
- Verifying the identity of every bulk chemical received before repackaging and completing a second identity test after repackaging
- Conducting regular tests of all chemicals in inventory
- Verifying all unique identifier numbers prior to shipping.

As a distributor and repackager of both Active and Non-Active Pharmaceutical Ingredients for pharmacy compounding, PCCA is registered and inspected by the FDA and DEA. The company is licensed in the state of Texas and all other states where licensure is required.

Click here to find out more about PCCA's quality processes.

Education

PCCA provides the Comprehensive Compounding Course (C3) and Aseptic Technique compounding course in our in-house training laboratories. These hands-on courses provide pharmacists and their pharmacy technicians with a

forum for learning the latest innovations in compounding unique dosage forms. In addition, the curriculum includes discussion of quality and safety procedures, legal issues, and marketing technique.

PCCA also conducts Accreditation Council for Pharmacy Education (ACPE)-accredited continuing education programs in the form of seminars and symposiums to provide pharmacists and physicians with ongoing opportunities to earn continuing education credit, practice compounding techniques according to USP <795> and <797> standards, and learn as effective methods of building patient and practitioner relationships. These programs also provide invaluable networking sessions where colleagues share what has worked well for their compounding practices and emphasize the critical importance of the triad relationship – the patient, prescriber and pharmacist.

Find out more about PCCA's educational offerings here.

Pharmacy Consulting

When pharmacists join PCCA, they gain access a staff of more than 30 pharmacists, PhDs, and chemists who fill a variety of roles, including consulting for members, R&D, and formulation development, ready to serve their technical support needs. On average, PCCA's Pharmacy Consulting Department answers more than 600 consulting calls a day from member pharmacists who have technical questions about preparing medications for patients.

Members and consultants have access to a database of more than 8,000 proprietary formulas that have been pre-tested with PCCA's fine chemicals and are continuously reviewed and updated. PCCA's staff draws upon a library of more than 600 pharmacy and medical references. All this adds up to the most comprehensive pharmacy consulting resource in the profession.

In addition to their consulting roles, PCCA's staff pharmacists also participate in ongoing ACPE-accredited training and educational courses, helping to educate prescribers and patients regarding the benefits of compounding. PCCA also maintains close, working relationships with several universities. In fact, PCCA is a dedicated rotation site for the University of Houston's College of Pharmacy.

Our Mission

PCCA's mission is to strengthen the role, position and skills of member compounding pharmacists so they can meet the unique healthcare needs of patients through our exceptional service, highest-quality products, shared innovations and education.

One patient. One prescriber. One pharmacist. A triad relationship with a common goal: achieving a positive therapeutic outcome for the patient. And in the midst of this relationship and this common goal is PCCA, the leader in pharmacy compounding since 1981.

Contact PCCA

Toll-Free 800.331.2498
Local: 281 933.6948
9901 South Wilcrest Drive
Houston, TX 77099

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- Compounding & Patients
- Talk to Your Doctor about Compounding
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Do Compounded Medications Require FDA Approval?

The FDA approval process is intended for mass-produced drugs made by manufacturers. Because compounded medications are personalized for individual patients, it is not possible for each formulation to go through the FDA's drug approval process, which takes years to complete and is prohibitively expensive, often costing hundreds of millions of dollars.

About PCCA

PCCA is an independent compounding pharmacy's complete resource for fine chemicals, devices, equipment, training & support.

Compounding Resources for Patients

We have created a number of online resources to help patients find answers to their most common questions:

- What is compounding?
- What are the benefits of compounding?
- What kinds of prescriptions can be compounded?
- What should I tell my doctor about compounding?
- What is PCCA?

Visit the Compounding Resources and Patients sections to find more.

Contact PCCA

Toll-Free 800.331.2466
Local: 281.933.8948
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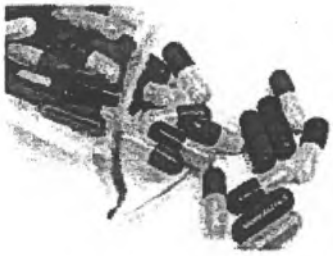
Compounding & Pharmacists

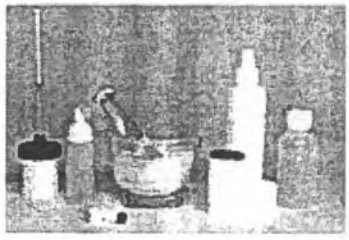
Pharmacists: Are you looking for a new direction?

Have you ever had a patient or a prescriber report that a patient had difficulty taking a medication as directed?

Do you wish you had more ways to use your pharmacy skills, knowledge, and creativity to work with your patients and prescribers to solve their unique medication challenges?

You're not alone! Pharmacy compounding has allowed many pharmacists to find their niche as medication problem-solvers. The "one-size-fits-all" nature of many mass-manufactured medications means that some patients' needs are not met by those products.





Many patients experience issues such as:

- Stomach upset when taking oral medication
- Reluctance to take the medication due to its taste
- Issues with the route of administration, such as difficulty swallowing pills
- Allergy, sensitivity, or other aversion to ingredients such as flavors or dyes, lactose, sugar, alcohol, gluten, or casein.
- Requiring a different dose of medication than that which is available from a manufacturer
- Difficulty keeping track of multiple medications
- Patients who need a medication that has been discontinued by the manufacturer
- Patients who don't want to take medication at all, especially children or pets

A compounding pharmacist may be able to provide solutions for challenges such as these. Working closely with the patient and the prescriber, compounding gives the pharmacist the means to customize medication to meet the individual needs of each patient.

At one time, all medications were compounded. Over the past few decades, compounding has experienced a renaissance as modern technology and innovative

techniques and research have allowed more pharmacists to customize medications to meet specific patient needs.

Learn more about what compounding and PCCA membership can do for your practice, your patients, and your prescribers!

Contact PCCA

Toll-Free 800.331.2498
Local: 281.933.6648
9901 South Wilcrest Drive
Houston, TX 77099

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Alternative Medication Forms

Unique medication delivery for your unique needs

Compounding enables prescribers and pharmacists to meet the special needs of patients. One of its most important benefits is to those patients who have difficulties with commercially available medication. With the prescriber's authorization, pharmacists can custom-prepare medications in a variety of unique dosage forms, including:

- Capsules
- Oral liquids
- Troches or lollipops
- Topical preparations
- Suppositories
- Eye and ear drops
- Nasal sprays
- Sterile injections

THE RESULT? A WAY TO TAKE MEDICINE THAT HELPS INCREASE PATIENT COMPLIANCE.

Custom Flavoring

Custom flavoring is available for most oral medication forms, and unique delivery systems may be employed to help give medication to finicky patients. Many medications can be taken through a flavored lollipop. Infants especially benefit from alternate delivery devices such as pacifiers or baby bottles. These devices, which are provided in child-proof packaging, allow parents to dispense prescription medicine easily and accurately.

Capsules

Medication can be compounded into customized capsules, especially in cases where an alternate strength is required or to omit potential allergens or irritants, such as dyes, preservatives, or gluten. To lessen the number of doses to be taken, multiple medications often can be combined into a single dosage or made into sustained-release capsules. Vegetarian capsules made from cellulose are available for patients who do not want to take a gelatin capsule.

Oral Liquids

Many medications can be compounded as oral liquids for those patients who have difficulty swallowing tablets and capsules. Some patients may have problems tolerating the taste of a commercially available liquid, but a compounding pharmacist can make a pleasant-tasting, custom-

flavored oral solution or suspension which can be administered easily and accurately. Some medications may be available as effervescent powders, which are mixed with water to make a fizzy drink.

Troches/Lollipops

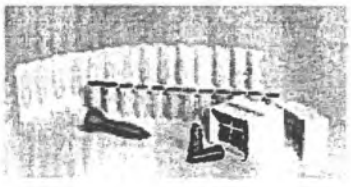
Troches and lollipops are used to keep drugs in the mouth when local action is needed there. Troches also may be placed under the tongue and allowed to dissolve, which allows the medication to enter the bloodstream quickly and easily. Some troches can be chewed and swallowed by a patient who cannot or will not take a capsule or tablet. These dosage forms can be enhanced with natural sweeteners and pleasant-tasting flavors, making them ideal for geriatric and pediatric patients.

Topical Preparations

Topical methods of delivery also are widely used because they allow the absorption of medicine directly through the skin, and may help avoid potential side effects such as stomach upset or drowsiness. Topical medications often are prescribed for pain management, inflammation and nausea/vomiting. They are easy to use and are effective delivering the medication as needed. Topical medication forms include:

- Gels
- Creams and lotions
- Sprays
- Foams
- Stick applicators, such as lip balms

Suppositories



Patients who cannot take medications orally are ideal candidates for compounded suppositories. Available in various shapes depending on the route of administration, suppositories can be given rectally, vaginally or urethrally. By melting or dissolving into the body cavity, they allow the medication to pass quickly into the bloodstream. They can be used for hormone replacement therapy (HRT), to fight nausea, or to treat local conditions such as hemorrhoids, infections, or inflammation.

A compounding pharmacist working closely with you and your physician can prepare medication in a dosage form that has been customized to your particular needs.

Ask your pharmacist today about alternate dosage forms and compounding.

Barbara Barnes

From:	Monte Lynn Jordan <mjresourceak@gmail.com>
Sent:	Monday, February 24, 2014 9:59 PM
To:	doa.drb.alaskacare.retiree.plan@alaska.gov
Cc:	sean.parnell@alaska.gov; curtis.thayer@alaska.gov; mike.barnhill@alaska.gov; Sen. Click Bishop; Sen. John Coghill; Sen. Pete Kelly; Rep. David Guttenberg; Rep. Scott Kawasaki; Rep. Tammie Wilson; Rep. Steve Thompson; Rep. Doug Isaacson
Subject:	Retiree Health Care Plan
Follow Up Flag:	Follow up
Flag Status:	Flagged

I am a retired State Employee. I worked for the State of Alaska for over 28 years. I own my home here. All of my three children were born and raised in Alaska - two of them graduated from UAF. I live in Alaska, full time and I always vote in borough, state and national elections.

It is my understanding that you are allowing public comments on the plan booklet until February 28, 2014. There are many significant problems with the Draft Retiree Benefit Book, and the State should allow at least an additional 60 days for sufficient review and input. This is an extensive document that is difficult to read and understand. Instead it should meet to the recommended readability grade level for U.S. Department of Labor Summary Plan Descriptions (6^{th} to 8^{th} grade).

To date the Draft has established the following unacceptable changes:

A new dental claim calculations based on Delta Dental standards for Alaska. This has changed the reimbursement calculation rates for out-of-network
claims from the 90^{th} percentile to the 80^{th} percentile, causing a much higher copay.

Teeth cleaning visits have been reduced from unlimited to one in every six-month period with limited exceptions.

There are many other examples of new limits and exclusions, including certain medications, eyeglass frames, lens options, decreased allowances

for travel costs, local anesthesia in surgery centers, etc.

There is a large increase in the number of procedures requiring pre-certification.

The Draft document lacks internal consistency. This makes it difficult to know whether a given procedure is allowed or disallowed.

This document does not clearly address how the State will carry out its fiduciary responsibilities for the retiree benefit Plan. It seems to delegate

authority for administering and designing the Plan to the third party administrators. Additionally, it takes the Division of Retirement & Benefits

completely out of the appeals process.

Clearly to rush this document to finalization will lead to future misunderstandings, problems and reveal a lack of concern for the detrimental effects on the benefits that it may have on the retired employees who need and count on the health benefits they worked for.

I believe an extension of at least 60 days is a reasonable request.

Sincerely,

Monte L. Jordan
Fairbanks, Alaska

Protecting, Promoting & Advancing Pharmacy Compounding

What is IACP?

International Academy of Compounding Pharmacists (IACP)

The International Academy of Compounding Pharmacists (IACP) is an association representing more than 3,600 pharmacists, technicians, students, and members of the compounding community who focus upon the specialty practice of pharmacy compounding. Compounding pharmacists work directly with prescribers including physicians, nurse practitioners and veterinarians to create customized medication solutions for patients and animals whose healthcare needs cannot be met by manufactured medications. More than 164,000 patients and prescribers also belong to our organization via the grassroots advocacy group, P2C2 (Patients and Professionals for Customized Care). IACP's mission of protecting, promoting and advancing personalized medication solutions is critical for patient healthcare. Visit www.iacprx.org to learn more and to find a compounding pharmacist near you.

IACP Mission

The mission of the International Academy of Compounding Pharmacists is to protect, promote and advance the art and science of pharmacy compounding.

IACP Vision

The International Academy of Compounding Pharmacists is the recognized authority for information, expertise, and practice standards with regard to pharmacy compounding.

More than 164,000 Voices Strong and Growing!

In addition, IACP represents more than 164,000 patients and practitioners including: physicians; veterinarians; and nurse practitioners through its ally grassroots organization, Patients & Professionals for Customized Care (P2C2). IACP is committed to ensuring the rights of physicians to prescribe, of pharmacists to prepare, and of patients to take personalized medication solutions that meet their unique, individual health needs.

As part of the free P2C2 membership, participants receive *Custom Care Times*, an electronic newsletter which is distributed monthly and covers a number of patient-centric topics, including the recent 17-P hydroxyprogesterone, a medication to help prevent pre-term labor.

Click here for more information about P2C2.

Contact Us

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Email: iacpinfo@iacprx.org

Protecting, Promoting & Advancing Pharmacy Compounding

What is Compounding?

Millions of patients have unique health needs that off-the-shelf, manufactured medications cannot meet. For these patients, personalized medication solutions – prescribed by licensed practitioners and prepared by trained, licensed pharmacists – are the only way to better health.

Working with a physician, a compounding pharmacist can meet individual needs of children, adults and animals. Whether it's an allergy to a dye or ingredient, a need for a different strength, or a preference for a different dosage form, compounding pharmacists provide patients with solutions to their medication needs.

Click below to listen to an interview with IACP's Excutive Vice President & CEO, David G. Miller, RPh, to learn more about pharmacy compounding.

As Heard on The Executive Report - US Airways In-flight Radio Show

Why Compounding?

When needed medication are discontinued by or generally unavailable form pharmaceutical companies, often because the medications are no longer profitable to manufacture;

When the patient is allergic to certain preservatives, dyes or binders in available off-the-shelf medications;

When treatment requires tailored dosage strengths for patients with unique needs (for example, an infant);

When a pharmacist can combine several medications a patient is taking to increase compliance;

When a patient cannot ingest the medication in its commercially available form and a pharmacist can prepare the medication in cream, liquid or other form that the patient can easily take; and

When medications require flavor additives to make them more palatable for some patients, most often, children.

How is it Regulated?

All pharmacies and pharmacists are licensed and strictly regulated by State Boards of Pharmacy. Compounding is a core component of pharmacy and always has been regulated by state boards, which are constantly updating their standards and regulations.

In addition, standards set by the United States Pharmacopeia (USP) are integrated into the practice of pharmacy compounding. The Pharmacy Compounding Accreditation Board (PCAB) has developed national standards to accredit pharmacies that perform a significant amount of compounding.

Compounding – The Numbers

1. The compounding industry now makes up an estimated 1 to 3 percent of the U.S. prescription market, which is $300 billion overall.
2. A national survey of independent pharmacists showed that 76 percent compound medications for patients.
3. Virtually 100 percent of hospitals compound medications.
4. Virtually all home health specialty pharmacies compound
5. All nuclear pharmacies compound.

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Email: iacpinfo@iacprx.org

Our Affiliates

Protecting, Promoting & Advancing Pharmacy Compounding

Frequently Asked Questions About Compounding

What is pharmacy compounding?

Pharmacy compounding is the customized preparation of a medicine that is not otherwise commercially available. These medications are prescribed by a physician, veterinarian, or other prescribing practitioner, and compounded by a state-licensed pharmacist. A growing number of people and animals have unique health needs that off-the-shelf, one-size-fits-all prescription medicines cannot meet. For them, customized medications are the only way to better health.

Who are compounding pharmacists?

Pharmacy compounding is a centuries-old, well-regulated and common practice. Pharmacy is one of the most respected and trusted professions in the United States. In a recent survey, pharmacists ranked second (only behind nurses) as the most trusted professionals in our society. Compounding has evolved into a specialty practice within the pharmacy community today. New applications to meet today's patient needs require additional education, equipment and processes that not all pharmacies possess.

Are compounded medications safe? How does one know that the compounded medication they are taking is safe and effective?

Compounded medications are similar to the so-called "off-label" use of FDA-approved drugs. When the FDA approves a specific drug as safe and effective, this determination applies only to the specific disease or condition for which the drug was tested. But physicians and veterinarians often prescribe medications for treatments for which they have not been specifically approved. Medical professionals do this because, in their judgment, the treatment is in the best interest of the individual patient. Similarly, medical professionals often prescribe compounded medications because they believe it is the best medical option for their patients. It is estimated that one fifth of all prescriptions written for FDA-approved drugs are for uses for which they were not specifically approved.

There are thousands of FDA-approved drugs on the market for just about any ailment. Why do we still need compounded medications?

Some valuable medications are available only by compounding. Restricting a doctor's access to compounded medications would be a serious mistake. Moreover, because of the economics of pharmaceutical manufacturing, FDA-approved drugs that serve a limited population are often discontinued by manufacturers. In most of these cases, the only option left for doctors and their patients is to have a compounding pharmacist make the discontinued drug from scratch using pharmaceutical grade ingredients.

What suppliers sell ingredients to compounding pharmacies? How are these suppliers regulated?

Just like big pharmaceutical manufacturing companies, compounding pharmacies get their ingredients for medications from suppliers that are registered and inspected by the FDA. Foreign suppliers are FDA-registered facilities.

How are compounding pharmacies and pharmacists regulated? Should there be increased federal oversight?

All pharmacies and pharmacists are licensed and strictly regulated at the state level. Compounding is a core component of pharmacy and has always been regulated by state boards, which are constantly updating their standards and regulations. In addition, standards set by the United States Pharmacopeia (USP) are integrated into the practice of pharmacy compounding. The Pharmacy Compounding Accreditation Board (PCAB) has developed national standards to accredit pharmacies that perform a significant amount of compounding.

Does the FDA have the expertise and federal power to regulate compounding pharmacies? Why shouldn't compounded medications, especially the most commonly used combinations, have to go through the FDA's established drug approval process?

The medical profession, including the practice of pharmacy, has always been regulated by the states. State boards of pharmacy are in the best position to inspect pharmacy operations, develop appropriate regulations and respond to problems or violations. The FDA does have an important role to play in making sure that ingredients used in compounding are safe and are manufactured by FDA-registered and inspected facilities, but there is no such thing as an "FDA-approved" pharmacy.

The FDA's drug approval process takes years and can cost hundreds of millions of dollars. Requiring this for individually personalized medications that fulfill an individual doctor's prescription is both impractical and contrary to the best interests of patients requiring immediate treatment.

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Our Affiliates

AMERICAN COLLEGE OF APOTHECARIES

Barbara Barnes

From: Sharon Gherman <scgherman@acsalaska.net>
Sent: Thursday, February 27, 2014 7:41 AM
To: doa.drb.alaskacare.retiree.plan@alaska.gov
Cc: sean.parnell@alaska.gov; curtis.thayer@alaska.gov; mike.barnhill@alaska.gov; Sen. John Coghill; Rep. Tammie Wilson

Subject: Comments on Proposed Changes to AlaskaCare Retiree Coverage

Follow Up Flag: Follow up
Flag Status: Flagged

Categories: Green Category

My name is Sharon Charnell Gherman. My address is 677 Eastview Drive, Fairbanks, Alaska 99712 and my phone number is 907.452.3677. My email address is scgherman@acsalaska.net. I am a PERS retiree with AlaskaCare benefits. My spouse, a TRS employee, is covered under my retirement health care plan, and will also be covered under his TRS retirement when he retires.

I have several comments about the proposed draft plan:

1. The comment period needs to be lengthened to allow adequate response from those affected.

2. **My biggest concern with the changes proposed in this plan is that it steers us into a preferred provider plan, which I strongly oppose.** I believe the greatest advantage of our AlaskaCare coverage as it has existed is the freedom to choose our providers and to travel freely to receive treatment. **I am absolutely opposed to preferred provider plan practices of requiring treatment at the closest facility offering the service.** If you want to go this way with future employees, fine, but you should not be significantly changing existing coverage for current retirees.

As an example of why we need the freedom to choose providers, my husband is a high school assistant principal who deals with conflict every day and is consequently pretty hard to anger. When preparing for a recommended but non-emergent sinus surgery, the head anesthesiologist at our local outpatient surgery center was so rude and arrogant to us that my husband walked out of the center, cancelled the surgery, and refuses for any of his family members to be treated there while that provider works there. **I am opposed to any change in the plan that would take away our freedom to choose our provider.**

3. I am opposed to the unrestricted power the proposed plan gives to Aetna to determine what treatment I receive or to veto or refuse to pay for the treatment my chosen provider recommends. My doctor should be the final authority for what treatment I should receive -- when we give authority to authorize benefit payment, we essentially give that non-medical individual the authority to determine what treatment I will receive. **Only my doctor should have that authority.**

4. Having just been through eight years of caring for a parent with dementia, I am opposed to restricting family members from being reimbursed for providing home health care under the policy. Family home health care providers fulfill a critical need that more and more of us will require, and they give up much to provide care for their loved ones. The least we can do is compensate them the same as a hired caregiver.

5. I am opposed to language that limits screening labs and radiological studies in the absence of "definite symptoms". Family health history or demographic data should be an acceptable reason to cover a screening. As an example, I am currently in the process of a surgery for a potentially life-threatening condition that was caught through screening - completely without "definite symptoms". Under this plan, my screening would not be covered.

6. If you intend to require precertification for so many additional procedures, then you should require the information that Aetna representatives provide over the phone to be binding.

7. **I am opposed to allowing retroactive dropping of coverage for any reason.** If someone is practicing fraud, pursue and collect damages from them. If they have earned their medical benefits, they should not be able to have them arbitrarily removed.

8. I am opposed to not covering lenses or frames unless the prescription changes. Glasses wear out and get scratched. Cover new lenses and frames every two years, period.

9. Massage therapy should be covered. I require far fewer chiropractic treatments when I receive a massage first. I know massage to be a very cost-effective treatment.

10. I oppose AlaskaCare benefits being secondary to Medicare Part B for Medicare-eligible retirees. Many, many physicians are refusing Medicare patients, and it threatens our ability to receive care. We need to stay away from anything that requires us to interact with the federal government health care system.

11. Prescription vitamins should be covered, as should compound drugs ordered by our provider. *Any* treatment prescribed by our chosen physician should be covered.

Thank you for the opportunity to comment on the proposed changes. PLEASE don't take us down the preferred provider road. We have had an excellent health care system that I believe will be viewed as a model for others down the road if we don't water it down and negotiate away its' strengths.

Sincerely,

Sharon Charnell Gherman

Fairbanks, Alaska

Protecting, Promoting & Advancing Pharmacy Compounding

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Our Affiliates

Barbara Barnes

From: Mary Calmes <yetna2@gmail.com>
Sent: Wednesday, February 05, 2014 1:16 PM
To: Mary Calmes
Cc: Rep. Scott Kawasaki; Sen. John Coghill; Sen. Pete Kelly; Sen. Click Bishop; Rep. Steve Thompson; Rep. David Guttenberg; Rep. Tammie Wilson
Subject: Issues of concern

Follow Up Flag: Follow up
Flag Status: Flagged

Categories: Green Category

Greetings Representatives and Senators from the Interior.

There are a few issues that have been of concern to me of late.

One issue is the governor's proposal to use **public monies to support private schools.** ***I am opposed to this on every level.*** I am NOT in any way associated with NEA, in fact I am a woman who opted to homeschool my sons. I also have no affiliation with religious institutions and hold firmly to separation of church and state. There is no reason in my mind why public monies should be provided to private schools.

Secondly, ***I support the state's proposal to give the Fairbanks North Star Borough the power to monitor and enforce state regulations on air quality.*** These are issues that are most effectively dealt with on the local level. We heat with wood and are more than willing to make the adjustments necessary to ameliorate our contribution to air pollution. We have found the borough's programs to encourage residents to make changes both compelling and generous. We value air quality and understand that we all need to be part of the solution.

As a retiree who is part of the State Health Care program, **I am concerned about the changes that have been made to the retiree health package.** The change to Aetna came with no announcement to those affected that a change was in the offing nor were the options being considered brought to light before decisions were made. Suddenly we are faced with choosing from a list of network providers, having to obtain permission for medical procedures, and with clear changes in approved medications. Health care coverage is complex and I am concerned that problems with the new coverage will only manifest themselves when folks have need for the care. We need to be provided with a clear understanding of how the change from HealthSmart to Aetna has affected our coverage. The state should be responsible for providing that information.

Thank you for your service to the people of the State of Alaska and in particular to those of us in the Interior.

Mary A Calmes

Mary & Tim
Fairbanks, AK

It has been said that man is a rational animal. All my life I have been searching for evidence which could support this.
-Bertrand Russel

AlaskaDispatch
News and voices from the Last Frontier
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Laurel Andrews [1]
February 28, 2014

Since the implementation of a new state health insurance plan on Jan. 1, Alaska has been battling with a retirees' group over changes in the new plan. Retired Public Employees of Alaska argues that the new plan, with details cloaked in confusing language, is reducing benefits, while the state contends that the changes don't reduce benefits and the old plan was in dire need of updating.

The plan hadn't been revised since 2003 and was "woefully in need of an update," said Department of Administration Deputy Commissioner Mike Barnhill. For the first time in more than a decade, a new draft document [2] was written up and presented to public employees.

The new plan has been called confusing by plan members who struggle to understand the changes. In the month of January, 50,000 phone calls were made to Aetna, Moda Health, and the Division of Retirement and Benefits call center combined, Barnhill said.

The state was hoping for more clarity, not less, Barnhill said. The state wrote in an FAQ for retirees that the 2003 plan "has been criticized for its lack of precision and clarity on a variety of issues. Many of the changes are intended to address this ... The Division will explore ways to provide explanatory documents that are more readable."

On Wednesday, following requests by RPEA, the state extended its comment period until April 30, two months after the comment period was to close originally.

The state is self-insured but contracts with a third-party to process its claims. Every five years, the state of Alaska opens that contract up, switching over the years between various third-party vendors. In January, it switched to Aetna.

Around 84,000 members -- roughly 68,000 of whom are retirees and their dependents -- are covered under state insurance, with 30,000 claims processed every week, Barnhill said.

The switch to Aetna has been marred by transitional issues that will be smoothed out in months to come, leading to the delay and re-sending of identification cards [3] and issues surrounding prescriptions. But those issues will be sorted out in time, RPEA president Jay Dunlay said. "It's the meat of the changes that the retirees are really concerned" about, he said.

RPEA hired consultant Freida Miller, who compared the old plan and new draft documents [4]. RPEA president Jay Dulany said that the union walked away with the perception of "significant reductions to (its) benefits coverage."

Most contentious are changes to the dental plan, which had not been administered by a third-party administrator before. The plan puts some caps on dental cleanings and determines both in- and out-of-network dentists. Folks who have in-network dentists -- roughly 60 percent -- likely received reduced bills, Barnhill said. Those with out-of-network dentists probably did see increased costs, Barnhill said.

Dental plans are fully funded by retirees, unlike medical plans, which are funded by the state. Barnhill said that the changes are intended to save the retirees money. Caps on dental cleanings were due to roughly 250 retirees who were getting between five and nine dental cleanings a year without examples of medical necessity, which hiked costs for the rest of members.

In its FAQ, the state writes that most of the changes in the new document were wording changes intended to eliminate ambiguity. Basic coverage, including deductible costs, pharmacy co-pay and medical coverages, haven't changed, the state said.

"There wasn't any intention to be any reduction in benefits," Barnhill said.

Retirees also worry about the new appeals process, which has been streamlined from four levels of appeal to three. The Division of Retirement and Benefits is no longer a party to appeals, and retirees wonder why. Barnhill said the new process will be more efficient and involves an independent medical review organization that will be an impartial party to appeal.

Dulany said he believes that the state is trying to decrease costs. The state is struggling with questions of unfunded liability of $12 billion [5] in its state retirement system, roughly $3.8 billion of which is health care costs.

"It certainly makes sense to try to reduce costs, but it doesn't make sense to do it on the backs of the retirees," Dulany said.

He added that the union will "try to enlist the entire retiree population" to put pressure on politicians to address the health insurance issue hand-in-hand with the unfunded liability issue.

Besides that, "the only other avenue that we have would be a legal (case)" Dulany said. That something they want to avoid, as "nobody wins" in that situation -- even if they win, attorneys' fees are taken out of the retirement fund. Still, it's not unprecedented for RPEA to pursue legal action. "We've done it in the past and we're not afraid to do it," Dulany said.

Meanwhile, the state is "trying as best we can to be responsive," Barnhill said.

Contact Laurel Andrews at laurel(at)alaskadispatch.com [6]. Follow her on Twitter @Laurel_Andrews [7].

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Barbara Barnes

From: Paul Harris <pgharris@gci.net>
Sent: Wednesday, February 05, 2014 1:22 PM
To: Rep. Tammie Wilson; emil.mackey@alaska.gov; roman.castro@alaska.gov; Sen. John Coghill
Cc: sean.parnell@alaska.gov
Subject: etna interpertation of perscription coverage for tier 1 retired employees

Follow Up Flag: Follow up
Flag Status: Flagged

Categories: Green Category

Once again with the change of insurance provider from Health Smart to Etna the Department of Administration is allowing Etna to interpret the benefits. The State has contracted with Etna to administer the insurance benefits it is the State's job to interpret what the benefits are.

For the past 4 (possible 5) years my wife has been using a compounded prescription that was prescribed by a health care provider. These specific compounded prescription was provided because of the side effects of over the counter medicines. Today we were told by North Pole Prescription Laboratory (an approved pharmacy under both Blue Cross and Health Smart), that the prescription benefit as administered by Etna would no longer cover these prescriptions. When I called the Etna health line they confirmed that these prescriptions were not covered. I was told that the only recourse was to file an appeal, a phone call is not sufficient, they would have to send me an appeals form in the mail. It seems that Etna does not have the ability to do conference calls with the Department of Administration so nothing can be resolved on the phone. So I called the Dept. of Administration Division of retirement and benefits. Roman Castro advised me that the problem was caused by the way Etna is interpreting the benefits and that I was not the only one having a problem with the interpretation Etna is using. Mr. Castro said that they had been instructed to tell people that had complaints to either email or write to Emil Mackey. That is what I am doing. Since for the past four years these prescription have been covered by our Health Insurance Prescription Policy; has the State reduced the insurance benefits provided to Tier 1 retirees receive or is Etna now controlling what benefits Tier 1 retirees can have?

The way I understand it is that the State of Alaska has contracted with Etna to administer the insurance benefits for the retired employees. Etna is paid to administer not interpret. It should not be Etna's job to determine what benefits the members get. Etna's job is to administer the payment of the benefits the State of Alaska has determined to be in affect. There has already been one attempt to change the benefits by the State and the Court has ruled that they could not make the change. In this case it appears that Etna has made the change either with or without the Department of Administration's approval. In either case the benefits that I have been receiving as a retired Tier 1 member have been reduced. This problem needs to be addressed and resolved quickly.

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Insurance nightmare

Terry Bradner Fairbanks | Posted: Wednesday, March 5, 2014 12:13 am

To the editor: I wonder how many state employee retirees have had as many problems as my family has in dealing with AETNA since their Jan. 1 takeover of the state's medical and dental insurance plan from AlaskaCare.

It has been a nightmare. Apparently their policy is to deny most payments and pressure caregivers, pharmacies and policy-holders to deal with those non-payments. Every doctor, pharmacist, caregiver and fellow retiree I've talked to has had trouble dealing with AETNA, so I believe the problem is pretty widespread.

In our particular case, my wife has had ongoing medical programs for more than a year and made incredible progress. Suddenly, after the first of the year when AETNA took over, we were told that all payments for medicine and treatments will be denied because of non-approval by the FDA. This is not true and has been documented. It's the reason AlaskaCare covered it last year.

The state even acknowledged in its newsletter that there is a major problem with AETNA. They are asking for member input online at doa.drb.alaskacare.retiree.plan@alaska.gov or by calling 1-800-821-2251.

I urge all state retirees to make their complaints known now. The state is obligated to its retirees. Many, like my wife, worked for years for the state with assurances that they would be provided for in their retirement years, with dignity. So far, I'm not seeing that with AETNA.

Barbara Barnes

From:	Mike Thurman <thurman@mosquitonet.com>
Sent:	Sunday, February 23, 2014 11:31 AM
To:	Rep. Tammie Wilson
Subject:	Draft AlaskaCare Retiree Benefit Plan Booklet - 3rd Try

Tammie, The first time I tried to sent this to you, it came back because of the attachment. I need a kid setting by my shoulder when I try to do something different on g-mail. I hope this is right now. Pat Thurman.

I'm sending you a copy of the e-mail I sent to DOA regarding the Draft Retiree Benefit Plan Booklet. Mike is a journeyman carpenter and belonged to the Carpenter's Union for years. Now he belongs to both RPEA and NEA-Retired

There are some questions which only the Legislators can put pressure on DOA to provide the answers. When "Rep. Munoz requested the Department of Law do an itemized analysis to determine the legal protection preventing medical diminishment of existing benefits, RPEA was informed she was told, ""It was too complicated to deal with"". If it's to complicated for the State's lawyers how does the State expect the retiree's to be able to determine if they're medical needs are going to be covered.

RPEA hired Frieda Miller, a former Manager of Benefits and Credentialed Health Care Specialist at Retirement and Benefits to compare the 2003 plan and the current plan. She has completed her task and issued her findings. to RPEA.

If you haven't received a copy of let me know and I'll forward it to you. I've started reading it and the appearance that the State turned over decisions to Aetna, which shouldn't be theirs to make, has been very disconcerting.

Regarding AlaskaCare draft Retiree Benefit Plan Booklet 2013

I attempted to read the draft Benefit Plan to determine if we would be receiving the same level of care we've had in the past. It is difficult to read because the language is confusing govermentize and there are contradictory statements. I did try to compare them to our old plan in the areas which most concerned us. Since it isn't laid out the same it made very difficult.

My husband,TRS Member, has Parkinson, a chronic condition. It appears that under **Section 3.4.13 Cognitive Therapy, Physical Therapy, Occupational Therapy and Speech Therapy Rehabilitation Benefits** his physical therapy and speech therapy wouldn't be cover. Parkinson, is a progressive disease and these therapies are a vital part of maintaining a his quality of life.

The comment period was very short on this plan. Please allow another 30 days for members to make comments.

Patricia A. Thurman, TRS Member

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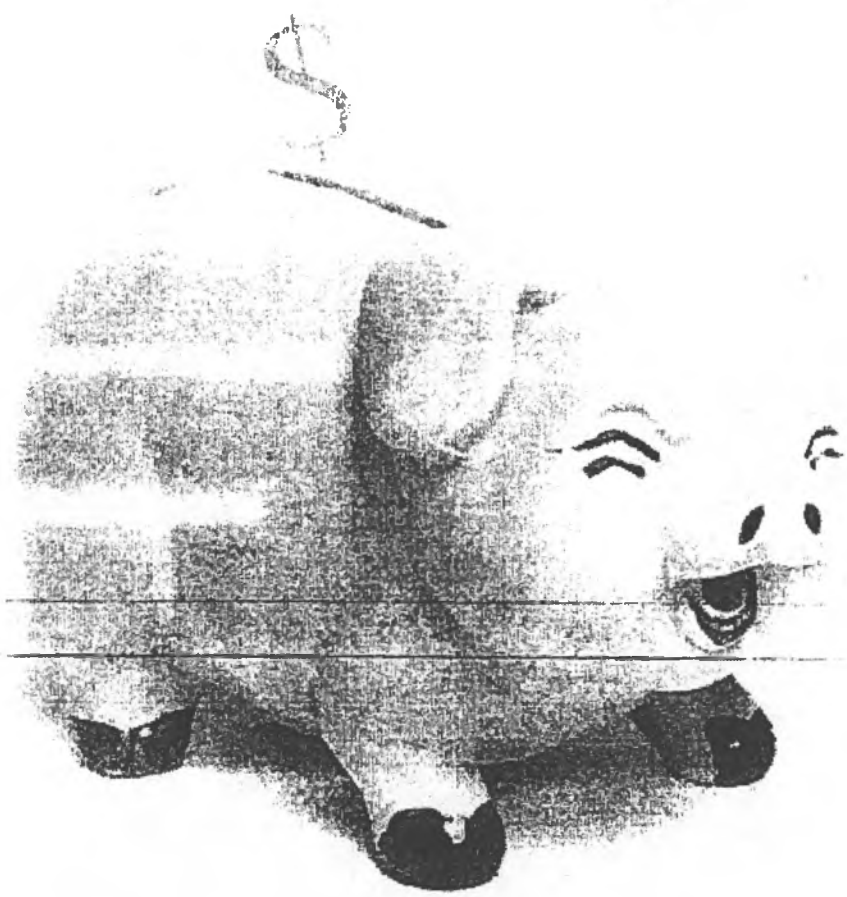
ESTRIOL:

Women's Choice vs. A Manufacturer's Greed

Jennifer Goodrum
International Academy of Compounding Pharmacists
Missouri City, Texas



ABSTRACT

The U.S. Food and Drug Administration recently took action to "halt" the compounding of hormone preparations that contain estriol, an action requested in a citizen petition filed by Wyeth Pharmaceuticals. If the Food and Drug Administration, with the support of Wyeth, is successful in its efforts, women throughout the U.S. who rely on compounded hormones containing estriol will have to discontinue their prescribed treatment. The International Academy of Compounding Pharmacists is engaged in ongoing outreach to ensure that members of Congress recognize the importance of protecting pharmacy compounding for the health and well-being of their constituents. Significant progress has been made with the recent introduction of a congressional resolution in support of estriol.

Estriol—one of three estrogens produced by the female human body—has been prescribed by healthcare providers and compounded by pharmacists for decades. Its use is accepted by all 50 state boards of pharmacy, the United States Pharmacopeial Convention, Inc. (USP), and the Pharmacy Compounding Accreditation Board (PCAB).[1] It is estimated that as many as 80%, if not more, of all compounded hormone preparations contain estriol.

In January 2008, the U.S. Food and Drug Administration (FDA) announced that it would "halt" the compounding of hormones that contain estriol. This announcement was made in the form of a press conference and a series of warning letters sent from the FDA to seven compounding pharmacies. The enforcement actions against estriol were requested in a citizen petition filed in 2005 by Wyeth Pharmaceuticals, maker of manufactured hormone products.

If the FDA's action is allowed to stand, it would force hundreds of thousands of women off of medications that their healthcare providers have prescribed for them—and for no scientific or medical reason. In its press conference announcing this action, the FDA admitted that its actions were not prompted by any adverse event or health issue associated with estriol, nor was the agency even aware of any such events or issues.

While estriol is not a component of an FDA-approved drug, it shares many of the characteristics of an approved drug, as follows:

- It has a long-standing USP monograph
- It has been used successfully and without problems for decades
- Its compounding is allowed by every state board of pharmacy
- It is approved and widely available in European and other countries
- It is a component of a drug now undergoing Phase II/III clinical trials

Congress has recognized that compounded medications may contain active ingredients with a USP monograph, even if they are not components of an FDA-approved drug. In addition, state boards of pharmacy, USP standards, and guidelines for compounding accreditation through the PCAB all permit the use of estriol.

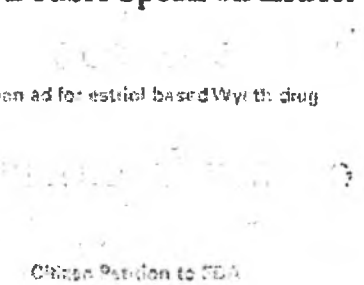
There does not appear to be a precedent for removing from the market a drug ingredient that has a USP monograph absent specific adverse events and health concerns. As such, the FDA's action appears to be directly related to Wyeth's petition to eliminate competition for its products.

WYETH PHARMACEUTICALS' INVOLVEMENT

Citizen Petition Against Compounded Hormones

Wyeth has played a significant role in this issue. On October 6, 2005, Wyeth filed a citizen petition with the FDA requesting actions that would severely restrict the availability of compounded hormone drugs, which are prescribed by licensed medical practitioners and prepared by pharmacists to meet patients' individual needs.

Wyeth Double Speak on Estriol



German ad for estriol based Wyeth drug

Citizen Petition to FDA

In its citizen petition, Wyeth stated that hormone drugs compounded with the human estrogen estriol "pose a serious threat to public health" and asked the FDA to take enforcement action against such preparations. According to the news website Pharmalot.com, however, "At the same time the petition was filed, Wyeth was selling Cyclo-Menorette, a menopausal drug, in four European countries (Estonia, Germany, Latvia, and Poland) that contained, yes, estriol." In fact, Wyeth called this product "the ideal therapy to enter into the years of change."

The FDA received a near-record 70,000 public comments in response to the petition, almost all from women and prescribers who wanted to preserve patients' access to compounded hormone therapies. Ignoring those comments, the FDA announced in January 2008 that it will restrict compounded hormones containing the one key form of estrogen. This is something Wyeth and its surrogates asked for in the petition. Unfortunately, the FDA's policy hurts women and helps Wyeth.

Groups and Experts Weighing in Against Compounded Hormones

Lack of Transparency on Their Part

Wyeth has funded a number of supposedly independent health organizations, many of which have publicly supported the company's campaign to restrict women's access to alternatives to its hormone products. Soon after Wyeth filed its citizen petition with the FDA, several organizations that purport to be independent filed public comments in support of Wyeth. In fact, though, each of these organizations has financial and other ties to Wyeth. Nearly all of the few comments filed in support of Wyeth's petition were from organizations with significant financial ties to Wyeth. Unfortunately, these organizations consistently fail to disclose their financial ties to the drug maker when voicing their support. Find out more at www.compoundingfacts.org.

Why is Wyeth Concerned about Alternatives?

The National Institutes of Health Women's Health Initiative (WHI) was cut short in 2002 after the results showed that Wyeth's synthetic hormone products increased the risk of strokes, breast cancer, heart attacks, and blood clots. According to Wyeth's annual reports, sales of Premarin-related products fell significantly, down almost 50% in 2007 from their peak in 2001. Restricting competition could help Wyeth bring its sales back to pre-WHI levels.

Wyeth's Campaign to Protect Market Share

Women's Health is Paying the Price

Wyeth Pharmaceuticals has a long history of campaigning before the FDA, as well as among media and policymakers, to restrict competition to its patented hormone products—Premarin

and Prempro—in order to protect its market share. Unfortunately, [illegible] need of hormone treatments to alleviate the uncomfortable and distressing symptoms of menopause.

Restricting Generic Hormones

According to a 1997 report from Citizens Against Government Waste (CAGW), a Washington, DC–based think tank, Wyeth waged a political campaign to influence the FDA's decision to keep a generic version of Premarin off the market. In this campaign, Wyeth asserted that its products could not be copied by generic manufacturers. Wyeth claimed that the active ingredients in the conjugated estrogen products could not be identified adequately and, therefore, that there can be no generic copy of Premarin because the precise characteristics of the drug cannot be characterized. Wrote CAGW:

> Although the FDA and Premarin's manufacturer, Wyeth-Ayerst, would like the American public to believe that this decision was in their best interests, the reality is that it was driven by hoards of lobbyists, fraught with conflicts of interest, and characterized by questionable 'behind-the-scenes political maneuvering.[2]

INTERNATIONAL ACADEMY OF COMPOUNDING PHARMACISTS TAKING ACTION

Understanding the high stakes and far-reaching implications of the FDA's actions against estriol, the International Academy of Compounding Pharmacists (IACP) has committed to the fight to preserve access to this therapy. Upon the FDA's January 2008 announcement of actions against estriol, IACP immediately sprang into action, performing a detailed legal analysis of the FDA's policy, exposing Wyeth's role in influencing the FDA's change in policy to [illegible] a massive grassroots letter-writing campaign to petition Congress and the FDA to alter this policy.

As a first step, IACP developed detailed legal arguments for why estriol is a permissible component of compounded medicines and why the FDA cannot prohibit the use of the term "bioidentical," another attack by the FDA in estriol warning letters. On February 5, 2008, IACP sent a detailed letter to FDA Commissioner Andrew C. von Eschenbach outlining these arguments and requesting a meeting to discuss the agency's new policy. IACP also provided the legal arguments as a resource to all IACP-member pharmacies that received warning letters from the FDA.

IACP worked with the American Pharmacists Association, the National Community Pharmacists Association, the National Alliance of State Pharmacy Associations, and the American College of Apothecaries to generate a joint letter to the FDA and Congress expressing the pharmacy profession's strong concerns over the FDA's decision and emphasizing the harm that this new policy would do to patients, forcing women who rely on compounded hormones to discontinue their prescribed treatments. The letter, signed by the five pharmacy organizations, was sent on February 1, 2008, to the FDA and Congress.

In mid-March, the FDA sent a notice to pharmaceutical suppliers informing them that the FDA will no longer allow them to distribute estriol to pharmacies or practitioners without an Investigational New Drug (IND) application. In response to this development, IACP organized a joint letter from the affected suppliers to the FDA registering their strong support for compounding and opposition to the agency's new restriction on estriol.

IACP also conducted meetings with staffers from key congressional offices, working with them to develop a congressional response to the FDA's actions. IACP members, constituents, and supportive members of the medical community have all met with congressional representatives to communicate the compounding community's position on the estriol issue.

IACP further organized a letter-writing campaign through the patient and prescriber advocacy organization for compounding, Patients and Professionals for Customized Care (P2C2). More than 10,000 patients, prescribers, and pharmacists have written letters to Congress and the FDA urging them to allow continued access to prescribed hormone treatments. For a comprehensive listing on everything that IACP is currently doing to help patients, providers, and pharmacists preserve access to estriol, visit www.iacprx.org/BHRTResources.

RECENT DEVELOPMENTS: IND APPLICATION FOR PRESCRIBING

Not long ago, the FDA adjusted its approach on estriol, clearly feeling the pressure from Congress, patients, pr[illegible]ers, and the pharmacy profession. The FDA now asserts that practitioners can prescribe compounded estriol but only if they file an IND application. However, IACP has a number of serious concerns with this proposal and does not consider IND filings to be a workable solution for the following reasons:

- The IND process was designed for manufactured drugs and is incompatible with compounded medications. It is impossible for prescribers to meet the voluminous data requirements for IND submissions. Initial applications must contain, for example, a detailed investigational plan; comprehensive clinical protocols; data on drug composition, manufacturing, and controls; toxicol-

Hormone	Naturally Occurring	Bioidentical
Estriol	$C_{18}H_{24}O_3$	$C_{18}H_{24}O_3$
Estradiol	$C_{18}H_{24}O_{24}$	$C_{18}H_{24}O_{24}$
Estrone	$C_{18}H_{22}O_2$	$C_{18}H_{22}O_2$
Progesterone	$C_{21}H_{30}O_2$	$C_{21}H_{30}O_2$

U.S. Food and Drug Administration on Bioidentical Hormone:

1 **FDA Myth:** The term "bioidentical" is misleading and "there is no credible science to back the claim that compounded hormones are biologically identical to the hormones produced by the body."[3]

Fact: Various professional medical societies define the term "bioidentical" as indicating that the chemical structure of a hormone drug is identical to that of the hormone produced by the human body. In the cases of estradiol, estrone, estriol, and progesterone, the term "bioidentical" accurately characterizes their chemical structure. They are all identical to those found in a woman's body.

2 **FDA Myth:** No Bioidentical hormone replacement therapy (BHRT) product has met federal standards for approval.

Fact: Since 1986, the FDA has approved at least 12 hormone replacement medications that are bioidentical and are marketed as such. Examples include Prometrium, a manufactured progesterone drug approved by the FDA in 1998 and marketed as bioidentical, and EstroGel, an estradiol product approved by the FDA in 2004, which is promoted as "an FDA-approved, bioidentical estrogen replacement therapy."

3 **FDA Myth:** It is unlawful for a pharmacist to prepare bioidentical hormones containing estriol because estriol is not a part of an FDA-approved drug.

Fact: A number of drugs are commonly compounded and prescribed even if they are not components of FDA-approved drugs. This practice is long-standing, well accepted, and legal in all 50 states. The use of estriol is consistent with United States Pharmacopeia (USP) standards for pharmacy compounding in chapters <795> and <1075>, and the USP is recognized by Congress as the official standards-setting authority for all prescription medications in the U.S. The use of estriol is also consistent with the standards of the Pharmacy Compounding Accreditation Board. The FDA admitted that it has received no reports of adverse events related to the use of estriol.

4 **FDA Myth:** Compounded bioidentical hormones are unsafe because they are not FDA-approved.

Fact: Compounded medications are regulated by state boards of pharmacy and are not subject to federal laws designed to regulate mass-produced drugs. This is because they are customized to meet the unique needs of a patient based on the specific orders of a healthcare provider. The FDA approval process is designed for mass-produced manufactured drugs. It is universally recognized that holding compounded medications to these standards would completely eliminate their availability.

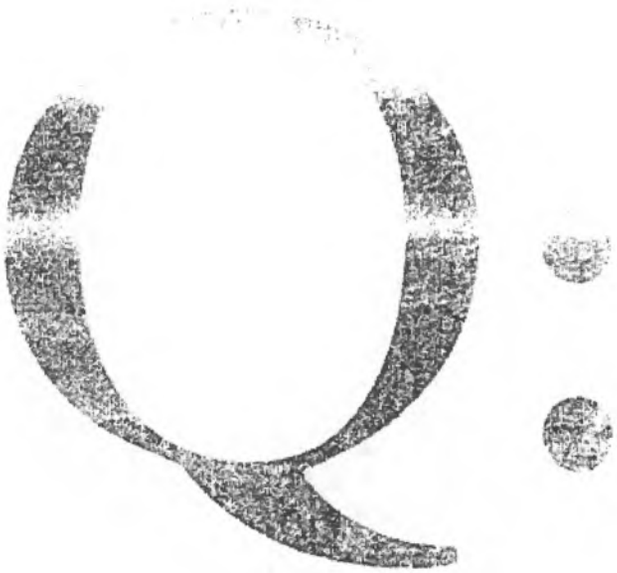
5 **FDA Myth:** BHRT is unregulated.

Fact: Bioidentical hormones—like all compounded medications—are made from FDA- and USP-registered materials—the same used by pharmaceutical manufacturers—and their preparation is well regulated by state boards of pharmacy that have responsibility for overseeing all pharmacy practice in each state. Pharmacies that compound medications, including bioidentical hormones, are regulated by state pharmacy boards—similar to the relationship prescribers have with their state medical board. There also are national standards and guidelines for compounded medications. The ingredients and their suppliers are regulated at the federal level by the FDA, with additional oversight provided by the USP.

IACP Common Questions and Answers on Estriol

Is the U.S. Food and Drug Administration (FDA) telling only seven pharmacies to stop compounding with estriol?

A: It is important to realize that the FDA's new policy against estriol does not affect only pharmacies that received warning letters. Steven Silverman, assistant director with the FDA's Office of Compliance, stated: "We expect...pharmacies [receiving warning letters] and other compounding pharmacies, unless they have an investigational new drug application, to stop compounding [preparations] including estriol." The International Academy of Compounding (IACP) strongly disagrees that pharmacies should have to discontinue compounding using estriol.



Is IACP supporting bad pharmacies?

A: IACP consistently advises its members to avoid making claims on websites and in marketing materials. IACP has marketing guidelines available to assist to this end. IACP does not support inappropriate claims; however, the FDA's warning letters go far beyond simply warning pharmacies for making inappropriate claims. The FDA states that the use of estriol in compounded medications is illegal and that the use of the term "bioidentical" is inappropriate. These actions affect all compounding pharmacies and must be vigorously fought.

Wasn't there an FDA-approved product available in the late 1970s that contained estriol?

A: There is a misconception that estriol was a component of a former FDA-approved drug product, Hormonin. While Hormonin was commercially available for a period of time and did contain estriol, the product never underwent the FDA approval process and provides no safe harbor. Another product that has been brought to our attention is Organon's Ovestin; however, this product does not appear to have approval in the U.S.

overview and pharmacology data and reviews of published scientific literature on the study drug. This information must be updated through information amendments, safety reports, and annual reports. Prescribers do not have the time or resources to undertake such a submission. Similarly, it would not be feasible for prescribers to undertake this for every compounded drug prescribed for every patient. These are appropriate tests for manufacturers to undertake in the process of bringing a new product to market, not for a practitioner prescribing an individualized, compounded medication for a particular patient.

- There are no streamlined IND procedures that would allow prescribers to submit an IND application for a compounded medication. Any such modifications to IND procedures would be subject to notice-and-comment rulemaking, and thus could not be immediately executed. As a result, prescribers cannot now use the IND process. It could be months or years before the FDA has the right procedure in place. In the meantime, women who are being prescribed hormones with estriol today would be forced to discontinue their treatment.
- Even if the FDA created a new IND procedure for compounded drugs containing estriol, this would not guarantee that women would continue to have access to these prescribed drugs. In fact, the FDA often refuses to even consider manufacturers' IND applications.
- A new IND procedure for compounded drugs containing estriol would only serve to further overwhelm the FDA's system. If thousands of prescribers file applications and request assistance with the new process, the FDA would be prevented from dealing with other INDs. And, if approval for IND applications for estriol is automatic, as the FDA has previously indicated, what is the rationale behind creating a substantial and unnecessary administrative burden for both prescribers and FDA staff?
- The purpose of an IND is to demonstrate the safety and effectiveness of a specific dose and particular dosage form of a drug that will be marketed in that same dose and form. Under an IND, a practitioner cannot prescribe a strength different than that authorized by the IND or adjust the dosing over time to fit a patient's needs. This is entirely inconsistent with the purpose of compounding, which is to provide individual patients with a customized dose and dosage form tailored to meet their personal needs.
- INDs require well-controlled, randomized clinical studies including a placebo or control arm. This means that some enrolled patients do not receive the desired drug. Some of the patients

seeking access to estriol-containing therapy through an IND will not receive the therapy they seek. Worse, because studies are usually blinded to eliminate bias, neither the patients nor their providers will know if they are receiving estriol. Women who are prescribed hormones with estriol expect to receive the drug that was prescribed for them. Indeed, to treat the debilitating symptoms of menopause, they need those drugs. Subjects who receive an IND drug typically are monitored very closely (e.g., multiple clinic visits, blood draws). While this process protects patients taking manufactured products that are being tested for safety and efficacy, these requirements will make participation inconvenient and unpleasant for patients taking compounded medications and would cause prescribers to incur huge costs. Again, these requirements are appropriate for new/investigational products coming to market but not for compounded medications.

- The FDA lacks the authority to enforce this policy. The agency claims to derive its authority over compounded medications from the Federal Food, Drug and Cosmetic Act (FDCA). It is this authority that it needs to require practitioners to submit IND applications in order to prescribe compounded hormones containing estriol. A federal court ruled, however, that the FDCA does not subject compounded medications to FDA authority and that it is not in "the best interest of the public health" to do so.

Clearly, the IND procedure does not provide a viable means by which women can receive the estriol that their providers are currently prescribing for them.

INTO THE FUTURE: LEGAL ALTERNATIVES AND CAPITOL HILL

IACP continues to explore legal and legislative options to address the FDA's policy [illegible] Due to ongoing litigation in the Midland case (*Medical Center Pharmacy, et al. v. Gonzalez*). At the heart of this case, which began in 2004 when ten pharmacies filed suit against the FDA for improperly criminalizing pharmacy compounding and preventing access to vital, legal bulk drug ingredients, lays the core issue of whether the FDA has authority to regulate compounding pharmacy. In 2006, the court ruled that compounded drugs for humans are not new, unapproved drugs and are not subject to FDA approval, and that pharmacies are exempt from FDA enforcement action. Regrettably, this decision has not brought much change in FDA's demeanor toward compounding pharmacies, as demonstrated by recent actions against estriol. The FDA continues to disregard rulings that are unfavorable to its positions against compounding. This case is currently under appeal and a decision may be issued as early as this summer. The ruling from this case will have a direct impact on the legal status of the FDA's new policy on estriol, and we are taking this into account as we assess our legal recourses.

On the legislative front, significant progress has been made in our campaign against the FDA's new policy to "halt" the compounding of compounded hormones containing estriol. In early May 2008, Representatives Mike Ross (D-Ark.) and Jo Ann Emerson (R-Mo.) introduced a Sense of the Congress resolution that raises direct concerns with the FDA's policy on estriol. The resolution, which includes original co-sponsors Tammy Baldwin (D-Wis.), Michael Burgess (R-Texas), John Carter (R-Texas), Sam Farr (D-Calif.), and Gabrielle Giffords (D-Ariz.), deems the FDA's policy "improper" and urges its reversal. The resolution also affirms that prescribers are in the best position to determine which medications are most appropriate for their patients and that the FDA should respect this important prescriber-patient relationship. Senator John Cornyn (R-Texas) and original co-sponsor Jim Bunning (R-Ky.) introduced a counterpart resolution in the Senate in early June.

This group of legislators has consistently demonstrated their support of pharmacy compounding, and this action is just the latest in a series of their efforts to protect patient access to [illegible]

DO YOUR PART!

IACP applauds those pharmacists who have already written letters to their members of Congress on this issue, but we continue to need your help. Please contact your Senators and Representative and urge them to support H.Con.Res. [illegible] and S. Con. Res. [illegible]. The more [illegible] the louder our message becomes. We need to preserve patient's access to estriol and options in womens' health. Take action today at www.SaveMyBHRT.org

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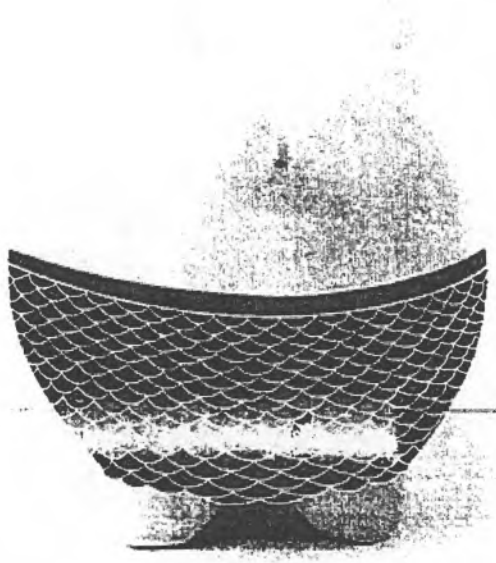

Natural Estrogens:

A REVIEW of the PRIMARY LITERATURE

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Published data support the potential benefits of estradiol and estriol.

The average age of women at menopause has remained approximately 50.4 years for centuries.[1] Thus, women today may spend 30% of their lives with reduced ovarian hormonal concentrations. It is estimated that 75% to 85% may develop symptoms secondary to this hormonal decline that may require some form of hormonal replacement.[1] For years this has been accomplished by supplementation with synthetic estrogens. Synthetic estrogens, by definition, are not the same biological chemicals that exist in our bodies from birth but are only imitations that have similar characteristics. Unfortunately, synthetic estrogens also cause many unwanted side effects. Recently natural estrogens have been the topic of much discussion among health professionals. The natural estrogens, which include estrone, estradiol and estriol, are made up of the exact biological chemical composition that has been part of the make-up of mankind for millennia. In theory, treating hormonal deficiencies with natural estrogens should have many benefits over synthetic estrogens. In fact, countless books have been written on the subject and currently many patients do take natural estrogens for hormonal supplementation.

Many health professionals realize that natural-estrogen supplementation could have advantages over synthetic-estrogen therapies but the apparent lack of literature on the subject, combined with the busy schedule of a typical health professional and the questions surrounding natural estrogens, limits their use. The purpose of this review is to provide answers to many common questions about natural-estrogen supplementation based on information found in the current primary literature. To accomplish this, a literature search was conducted from 1966 through 1999 using the National Library of Medicine database, Medline. The most recently published studies were chosen for this review based on their ability to answer one of many common questions about natural estrogen replacement. Common inquiries include questions about cardiovascular effects, lipid metabolism, blood-clotting effects, bone resorption, urinary tract infections and skin aging. Other common questions address concurrent disease states such as hypertension and diabetes or routes of administration and dosage schedules. A brief synopsis discussing these issues forms the body of this review. Hopefully, this information will help physicians and pharmacists make the best professional choices for their patients concerning estrogen replacement therapy.

Cardiovascular Effects

Estradiol has a positive cardiovascular effect on postmenopausal women. The positive effects can be reached by using 2 mg/day of estradiol orally, 1 mg/day of estradiol sublingually or 50 µg/day transdermally. Patients will benefit even if they already have cardiovascular disease or have had a hysterectomy.[1-6]

Snabes and colleagues conducted a randomized, double-blind, placebo-controlled, crossover study of 31 healthy postmenopausal women volunteers to examine the effects of estradiol replacement therapy on cardiac structure and function. Subjects were given 2 mg of micronized estradiol or a placebo orally for 12 weeks, at which time echocardiography and Doppler techniques were used to assess the cardiac effects. Snabes and colleagues found that, while estradiol serum concentrations rose fifteenfold to 37.6 pmol/L, the treatment did not affect measurements of systolic function, diastolic function, left ventricular mass or pulmonary artery pressure at rest or during physical exertion ($p<0.01$). They concluded that estradiol replacement therapy, which results in physiologic serum concentrations, does not affect cardiac structure or function in normal postmenopausal women after 12 weeks of treatment.[2]

Rosano and colleagues conducted a randomized, double-blind study to examine the effect of estradiol on exercise-induced myocardial ischemia in women with coronary artery disease. Eleven women with confirmed coronary artery disease were given 1 mg of sublingual estradiol or a placebo 40 minutes prior to a treadmill exercise test. The time to 1 mm ST segment depression ($p<0.004$) and total exercise time ($p<0.01$) was increased by estradiol. Rosano and colleagues hypothesized that estradiol could lessen myocardial ischemia by reducing myocardial oxygen consumption through a decrease in the peripheral vascular resistance or by lowering preload. A possible alternative mechanism is a direct vasodilator effect on the coronary arteries. The authors concluded that this therapy could be a useful new treatment or an adjunct to existing therapy for stable angina in women. They also felt that this study may help explain some of the protection against coronary artery disease apparent in women before menopause and the protective effects of estradiol replacement therapy in postmenopausal women.[3]

Three other studies confirm the conclusions of Snabes and Rosano. The first, conducted by Volterrani and colleagues, also used 1 mg of sublingual estradiol and achieved similar results ($p<0.05$). Interestingly, six of the 11 patients in this study had undergone a hysterectomy.[4] The second, conducted by Riedel and colleagues, used blood-flow rates of the left common femoral artery in 23 postmenopausal women as an outcome measure of vascular response to 1 mg of sublingual estradiol. Estradiol induced a vasodilation of the femoral arteries compared to basal and placebo

measures (p<0.001).[5] The third, conducted by Cacciatore and colleagues, studied the long-term effects of oral and transdermal hormone replacement therapy (HRT) on carotid and uterine vascular impedance. This trial, which was conducted for one year, followed an open, randomized, controlled design and involved 63 postmenopausal patients who were assigned to use either estradiol 2 mg/day orally or transdermal estradiol 50 µg/day. Cacciatore and colleagues showed that both oral and transdermal estradiol are virtually identical in their ability to reduce carotid and uterine artery resistance to blood flow (p<0.001). They concluded that this long-term vascular effect may explain how estradiol protects women from cardiovascular disease.[6]

Lipid Metabolism

Estradiol has many positive effects on lipid metabolism. Estradiol, given orally or transdermally, reduces low-density lipoprotein (LDL) and very-low-density lipoprotein (VLDL) cholesterol levels. In postmenopausal women, and even women who have had a hysterectomy, estradiol has been shown to reduce lipoprotein (A) (Lp(A)) levels, which are associated with an increased risk of coronary artery disease and cerebrovascular accidents. Doses of transdermal estradiol are critical to produce these positive effects and need to be at least 1 mg/day or higher to demonstrate this biological activity.

Karjalainen and colleagues investigated changes in plasma lipid and lipoprotein levels induced by oral estradiol valerate and transdermal estradiol gel in a controlled, double-blind, double-dummy study. The patients were 79 hysterectomized postmenopausal Caucasian women who were seeking hormone substitution therapy for climacteric symptoms. Patients received 2 mg/day of oral estradiol valerate or applied 1 mg of topical estradiol gel daily at bedtime. In the estradiol valerate group, total and LDL cholesterol were decreased and high-density lipoprotein (HDL) cholesterol and triglycerides were increased (p<0.001). In the estradiol gel group, plasma total, LDL and VLDL cholesterol and the ratio of LDL/HDL cholesterol were significantly decreased (p<0.001), but no change in HDL cholesterol and triglycerides was observed.[7] No serious adverse events related to the study treatments were noticed. Mild skin irritation was reported by three women in the oral placebo group and two in the estradiol gel group. Breast tenderness was reported by 14 women in the oral estradiol treatment group and eight women in the transdermal estradiol treatment group.

Haines and colleagues studied oral estradiol treatment to see if it was effective in lowering concentrations of Lp(A). The Lp(A) level is an independent risk factor for premature coronary artery disease and cerebrovascular accidents. Concentrations of this lipoprotein tend to increase after menopause. A double-blind, placebo-controlled, crossover study was conducted during a 12-month period in 100 postmenopausal women who had undergone hysterectomy. The women were randomized into two groups: group one received oral estradiol, 2 mg/day, for the first six months and placebo for the second; and group two received these treatments in the reverse order. Crossover analysis showed a 9.62% reduction in values of Lp(A) with estradiol treatment compared with a placebo during 12 months of treatment (p<0.001). No major side effects were noted.[8]

Elkik and colleagues studied the effects of percutaneous estradiol and conjugated estrogens on the level of plasma proteins and triglycerides in 18 postmenopausal women. Patients were randomized to receive either conjugated estrogens orally, 1.25 mg/day, or transdermal estradiol ointment 3 mg each evening. Both treatments were biologically effective and plasma triglycerides tended to increase in the conjugated estrogen group and to decrease in the transdermal group, though not significantly. However, plasma renin substrate and antithrombin III increased significantly (p<0.01) in the conjugated estrogen group. The authors concluded that the lesser toxicity of transdermal estradiol could be partially explained by the route of administration, since transdermally estradiol bypasses the liver. No major side effects were noted.[9]

Two other studies that were both conducted by Walsh and colleagues seem to contradict the conclusions of Elkik and colleagues. Walsh and colleagues conducted two studies comparing oral estrogens with transdermal estradiol in a dose of 0.1 mg applied twice weekly. These researchers concluded in each study that transdermal estradiol was ineffective in producing any positive effects on plasma lipoproteins. The conclusions are very suspicious and should not be taken seriously because the dose of transdermal estradiol was subtherapeutic. This is further supported by the fact that Walsh and colleagues never checked for estradiol blood levels in their studies; whereas Elkik and colleagues, Haines and colleagues and Karrjalainen and colleagues all conducted some form of double check to see if the treatments were biologically effective.[7-11]

Blood-Clotting Effects

Antithrombin III is the primary inhibitor of blood coagulation and its congenital deficiency is associated with severe and recurrent venous thrombosis. The association of oral contraceptive drugs and thrombosis has been known for a long time. Estrogen therapy has been considered a risk factor for thromboembolic events, especially in women with other risk factors such as antithrombin III deficiency. The key to preventing this adverse effect of estrogen therapy is to choose the correct route of administration. Oral estrogen therapy, supplanted with natural or synthetic hormones, will cause negative changes in coagulation and fibrinolytic parameters.[12-13] However, transdermal estrogen therapy does not modify these parameters and would be the preferred route of estrogen administration for women at risk for thromboembolism.[12]

Bonduki and colleagues conducted a prospective, randomized study to evaluate antithrombin III levels in 19 postmenopausal women receiving hormonal replacement. The patients received either continuous daily oral conjugated estrogen 0.625 mg or estradiol transdermally 50 µg daily. The antithrombin III levels in the conjugated estrogen group declined significantly (p<0.05), but the transdermal estradiol group remained unchanged.[12] In a double-

blind, randomized, prospective study, Conard and colleagues compared a placebo and oral micronized estradiol 2 mg/day during a six-month period. They found that, compared with a placebo, oral estradiol therapy resulted in a significant decrease in fibrinogen and a significant increase in plasminogen.[13] These conclusions are also supported by the work of Elkik and colleagues and their comparison of oral and transdermal estrogen therapy.[9] Therefore, transdermal estradiol administration may be more beneficial in terms of coagulation than oral conjugated estrogen therapy, especially in women with predisposing factors to thrombosis.[9,12]

Bone Resorption

Estradiol has a positive effect on the biochemical markers for bone resorption and on bone mineral density in oral and transdermal dosage forms.[14-16] Estriol may also have a positive effect on bone mineral density. However, estriol may not be as effective in reducing bone resorption in women with a history of hysterectomy.[17,18] No matter what dosage form of estrogen is chosen to prevent bone loss, it does seem clear that adjunctive therapy with some form of calcium supplementation is vital.

Reginster and colleagues, in a controlled, randomized group comparison, compared the effects of oral conjugated estrogen 0.625 mg/day and transdermal estradiol 50 µg/day on biochemical markers of bone resorption in 60 healthy menopausal women. In both groups they found that, after three months of therapy, hydroxyproline/creatinine ratios were significantly ($p<0.05$) reduced. Pyridinoline/creatinine ratios were also significantly ($p<0.01$) reduced. They concluded that both therapies were equally effective in reducing postmenopausal bone resorption. Five patients withdrew from this trial because of mastodynia and weight increase.[11]

Ettinger and colleagues studied low-dose oral estradiol in a double-blind, randomized, dose-ranging design. Over an 18-month period they studied the protective effects of dosages of 0.5 mg, 1 mg and 2 mg in 41 postmenopausal women. Each patient was also given 1500 mg of calcium carbonate daily. Using bone-density measurements, they concluded that micronized estradiol, taken orally, has a continuous skeletal dose-response effect in the range of 0.5 mg/day to 2.0 mg/day and that calcium intake positively modifies the skeletal response. No serious side effects were noted.[15]

Evans and colleagues studied low- and conventional-dose transdermal estradiol in 169 postmenopausal women with bone-status problems. Patients were given either 25 µg or 50 µg of topical estradiol daily. Bone mineral density was the main outcome measure; the authors concluded that transdermal estradiol is effective in preventing spinal bone loss at all postmenopausal ages and is capable of doing this in low dosages. Prevention of bone loss at the femoral neck is less certain and the average change in bone mineral density over three years was significantly lower ($p<0.001$) than in the lumbar spine. Evans and colleagues also found that the use of estradiol 50 µg/day is not associated with a greater response in bone mass. No significant side effects were noted.[16]

The effects of estriol on bone resorption have also been studied. Minaguchi and colleagues, in a multicenter, prospective, open trial, studied the effects of oral estriol on bone mineral density and bone metabolism in postmenopausal women. They treated 75 women for 50 weeks with 2 mg/day of estriol and 0.8 g/day of calcium lactate. They found that after 50 weeks the women's bone mineral density had increased 1.79% ($p<0.01$) compared to pretreatment levels.[17] In contrast, Devogelaer and colleagues found that oral estriol in a dose of 2 mg/day did not maintain bone mass, whereas 1.5 mg/day of estradiol did counteract bone loss. This may seem controversial but Devogelaer and colleagues studied hysterectomized women who did not receive any calcium supplementation during the two-year, double-blind study.[18] These changes in baseline calcium supplementation, combined with the different patient population, may explain the controversy.

Urinary Tract Infections

An estimated 10% to 15% of women more than 60 years of age have frequent urinary tract infections. Hormonally induced changes in the vaginal flora associated with menopause are thought to play an important part in the pathogenesis of urinary tract infections in older women. Estriol has been shown to be very effective at reducing chronic urinary tract infections and, when administered topically, works faster than when taken orally.[19-20]

Raz and Stamm studied 93 postmenopausal women with a history of recurrent urinary tract infections in a randomized, double-blind, placebo-controlled trial of a topically applied intravaginal estriol cream. Patients received 0.5 mg of estriol in a vaginal cream to be applied once each night for two weeks, followed by twice-weekly applications for eight months; the other group used a placebo cream in the same manner. The incidence of urinary tract infections in the estriol group was significantly reduced ($p<0.001$), compared with that in the placebo group. Lactobacilli were absent in all vaginal cultures before treatment and reappeared after one month in 61% of the estriol-treated women but in none of the placebo recipients ($p<0.001$). With estriol the mean vaginal pH declined from 5.5 to 3.8 ($p<0.001$), whereas there was no significant change with placebo. Ten women withdrew from this study because they experienced local side effects from the estriol treatment.[19]

Kirkengen and colleagues, in a block-randomized, double-blind, group-comparative, placebo-controlled study, assessed the effect of oral estriol on recurrent urinary tract infections in 40 postmenopausal women. Women were given a single morning dose of estriol 3 mg/day the first four weeks and 1 mg/day during the last eight weeks of the study or a matching placebo. During the first four weeks, there was no difference between estriol and placebo treatment. However, after four weeks of therapy, oral estriol therapy was significantly more effective ($p=0.05$) at reducing the number of urinary tract infections. No significant side effects were noted.[20]

Skin Aging

The coincidence of climacteric symptoms and the beginning of skin aging suggests that estrogen deficiency may be a common and important factor in the perimenopausal woman. Topical estradiol 0.01% and estriol 0.3% both combat the onset of skin aging. Schmidt and colleagues investigated whether topical treatment of the skin with estrogen could reverse some of the changes in the aging of skin. In this open-label study, 59 women applied 1 g of either 0.01% estradiol cream or 0.3% estriol cream daily for six months. The effects were compared with preclimacteric women with skin-aging symptoms. After treatment for six months, elasticity and firmness of the skin had markedly improved and the wrinkle depth and pore sizes had decreased by 61% or more in both estrogen groups ($p=0.05$). Furthermore, skin moisture and the number of collagen fibers had increased. No systemic hormonal side effects were noted.[21]

Hypertension

After menopause, both systolic and diastolic blood pressure become higher in women than in men of the same age, suggesting that estrogen deficiency may influence the age-related increase in blood pressure. Transdermal and oral estradiol both have blood pressure-lowering properties in postmenopausal women. Mercuro and colleagues studied 30 postmenopausal women affected by mild hypertension in a randomized, double-blind protocol. Subjects received patches of transdermal estradiol that delivered 100 µg/day or a matching placebo. Administration of estriol significantly ($p<0.05$) decreased 24-hour systolic and diastolic blood pressure and did not cause any side effects.[22] The effect of oral estradiol on blood pressure was examined by Van Ittersum and colleagues. In their randomized, controlled trial, 29 women were treated with 1 mg of estradiol daily and compared with a group that did not receive treatment. Changes in blood pressure differed significantly ($p=0.05$) between the two groups after one year. A decrease of more than 5 mm Hg was observed in the estradiol group, whereas an increase was found in the control group. No significant side effects were noted.[23]

Diabetes

Estrogen replacement therapy is associated with a decreased risk of cardiovascular disease in postmenopausal women. Patients with noninsulin-dependent diabetes mellitus have an increased cardiovascular risk. However, estrogen replacement therapy is only reluctantly prescribed for patients with noninsulin-dependent diabetes mellitus. Estrogen therapy should be prescribed in this population. Estrogen therapy administered orally and transdermally improves sensitivity in the liver, glycemic control, lipoprotein profiles and fibrinolysis in postmenopausal women with noninsulin-dependent diabetes mellitus.[24,25] Brussaard and colleagues, in a double-blind, randomized, placebo-controlled trial, studied the effect of 2 mg of oral estradiol given daily over six weeks in 40 postmenopausal women with noninsulin-dependent diabetes mellitus. The estrogen-treated group demonstrated a significant ($p<0.03$) decrease of hemoglobin bA1/c, LDL cholesterol, and apolipoprotein B levels.[24] In an open-label, randomized, crossover study, O'Sullivan and Ho compared the effects of oral and transdermal estrogen replacement on glucose tolerance. Nine patients were randomized to receive either 100 µg/day of transdermal estradiol or 1.25 mg/day of conjugated estrogen for 12 weeks and then crossed over to receive the alternative treatment for another 12 weeks. The authors found that mean glucose and insulin levels were maintained at an identical level during the hyperinsulinemic euglycemic clamp performed at pretreatment and during estrogen therapy. They concluded that the route of estrogen replacement therapy does not have a major impact on glucose metabolism in postmenopausal women. No significant side effects were noted.[25]

Conclusion

Estradiol and estriol have many potential benefits. Estradiol has a positive cardiovascular effect that can be achieved by using 2

mg/day orally, 1 mg/day sublingually or 50 µg/day transdermally.[2-6] Estradiol has been shown to reduce LDL, VLDL and Lp(a) when given orally or transdermally.[7-11] Transdermal estradiol also lowers antithrombin III levels, which are associated with severe and recurrent venous thrombosis.[9,12-13] Estradiol has a positive effect on bone mineral density in oral and transdermal dosage forms.[14-16] Chronic urinary tract infections can be reduced by supplementing estriol, which, when applied topically, works faster than when taken orally.[19-20] Estradiol has a positive effect on skin aging,[21] lowers blood pressure,[22-23] and improves glycemic control in patients with noninsulin-dependent diabetes mellitus.[24-25] Armed with this information, physicians and pharmacists can make well-informed professional decisions about estrogen replacement therapy for their patients.

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