



California State Board of Pharmacy

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STATE AND CONSUMERS AFFAIRS AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
ARNOLD SCHWARZENEGGER, GOVERNOR

Contact Person: Patricia Harris
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LICENSING COMMITTEE MEETING

March 22, 2006

**Hilton Oakland Airport
One Hegenberger Road
Oakland, CA 94621
(510) 635-5000**

9:30 a.m. – 12 noon

MEETING MATERIALS

Agenda Item 1

Request to amend 16 CCR § 1728 to increase the number of intern hours that can be earned outside a pharmacy

Agenda Item 2

Request from the Accreditation Commission for Health Care, Inc. (ACHC) and the Community Health Accreditation Program (CHAP) to renew the board's approval as accreditation agencies for pharmacies that compound injectable sterile drug products pursuant to Business and Professions Code section 4127.1(d)

Agenda Item 3

Recommendation to add a regulation that recognizes the approved accreditation agencies for pharmacies that compound injectable sterile drug products and include in the regulation the criteria used to approve the accreditation agencies

Agenda Item 4

Request to extend the waiver for the study by the UCSF School of Pharmacy and Cedars-Sinai Medical Center entitled, "Evaluation of the Impact of Pharmacists in the Prevention of Medication Errors Associated with Prescribing and Administration in the Hospital Setting"

Agenda Item 5

Announcement by the National Association of Boards of Pharmacy (NABP) regarding the evaluation process of foreign pharmacy graduates

Agenda Item 6

Announcement by the Accreditation Council for Pharmacy Education (ACPE) regarding changes to its accreditation procedures

Agenda Item 7

Competency Committee Report

AGENDA ITEM 1

Memorandum

To: Licensing Committee

Date: March 9, 2006

From: Patricia Harris 
Executive Officer

Subject: Request to increase the number of intern hours that
can be earned outside of a pharmacy

At the February meeting, the board was provided with a proposal from a group of pharmacy students representing various schools of pharmacy requesting an increase in the number of intern hours that could be earned outside a pharmacy. Since the proposal was not on the agenda, the board could not take action.

The proposal is now being provided to this committee for consideration. The proposal requests that the board allocate up to 400 hours that an intern can earn for pharmacy-related experience (under the supervision of a pharmacist) outside a pharmacy. The proposal is attached.

Under current law, an intern must earn a minimum of 900 hours of pharmacy experience under the supervision of a pharmacist in a pharmacy. The board has the discretion to grant a maximum of 600 hours for other experience substantially related to the practice of pharmacy. California pharmacy students earn the 600 hours for school required experiential training (clinical clerkship).

Therefore as proposed, an intern would only need to earn a minimum of 500 hours in a pharmacy and could earn a maximum of 1,000 hours of experience substantially related to the practice of pharmacy under the supervision of a pharmacist.

16 CCR § 1728 states in part:

(a) Prior to receiving authorization from the board to take the pharmacist licensure examinations required by section 4200 of the Business and Professions Code, applicants shall submit to the board the following:

(1) Proof of 1500 hours of pharmacy practice experience that meets the following requirements:

(A) A minimum of 900 hours of pharmacy practice experience obtained in a pharmacy.

(B) A maximum of 600 hours of pharmacy practice experience may be granted at the discretion of the board for other experience substantially related to the practice of pharmacy.

(C) Experience in both community pharmacy and institutional pharmacy practice settings.

(D) Pharmacy practice experience that satisfies the requirements for both introductory and advanced pharmacy practice experiences established by the Accreditation Council for Pharmacy Education.

DRAFT

**RESOLUTION FOR CONSIDERATION BY THE
CALIFORNIA STATE BOARD OF PHARMACY**

WHEREAS the scope of practice opportunities in the profession of pharmacy has expanded beyond the traditional areas of community and institutional pharmacy, and

WHEREAS the increased scope of pharmacy based opportunities exist for pharmacy school graduates in such areas as the pharmaceutical industry, managed care; regulatory affairs, and other pharmacy-related areas to yet be defined, and

WHEREAS the present existing laws place requirements on both the experience expectations and the quantity of time required of students enrolled in California Schools of Pharmacy in order for them to satisfy both the board exam and licensure standards as stated in the following California statutes and regulations:

CA Bus. & Prof. Code, Sec. 4200(a)(5): "The board may license as a pharmacist any applicant who meets the following requirements... Has completed 1,500 hours of pharmacy practice experience or the equivalent in accordance with Sec. 4209."

CA Bus. & Prof. Code, Sec. 4209(a)(1)(2): An intern pharmacist shall complete 1,500 hours of pharmacy practice before applying for the pharmacist licensure examination. This pharmacy practice shall comply with the Standards of Curriculum established by the Accreditation Council for Pharmacy Education or with regulations adopted by the board.

Title 16, CA Code of Regulations, Sec. 1728(a): ...Applicants shall submit to the board the following: Proof of 1,500 hours of pharmacy practice experience that meets the following requirements:

(A) A minimum of 900 hours of pharmacy practice experience obtained in a pharmacy.

(B) A maximum of 600 hours of pharmacy practice experience may be granted at the discretion of the board for other experience substantially related to the practice of pharmacy.

(C) Experience in both community pharmacy and institutional pharmacy practice settings.

(D) Pharmacy practice experience that satisfies the requirements for both introductory and advanced pharmacy practice experiences established by the Accreditation Council for Pharmacy Education. And

WHEREAS while the American Council on Pharmaceutical Education (ACPE) does support that the Schools of Pharmacy engage students during the experiential portions of its academic program in various patient care settings, it also encourages other extended boundaries of learning during the experiential portion of the academic program. Under Standard No. 14 (Curricular Core: Pharmacy Practice Experiences), Guideline 14.1 it states the following:

“The scope, intensity, and duration of all of the pharmacy practice experiences should afford students the opportunity to develop skills consistent with expected professional competencies and outcomes. The pharmacy practice experiences should ensure that every student has multiple opportunities to perform pharmaceutical/patient-centered care activities in a variety of settings (including acute care, long-term care, home care, community, ambulatory, administrative)...” And

WHEREAS all students who undergo the pharmacy curriculum at the University of Southern California School of Pharmacy have multiple pharmacy-related experiences that might include managed care and industrial pharmacy settings that count toward their 600 required hours of experiential training, those areas of experiences that are more directly patient based are assessed by the use of competency criteria once established by the California State Board of Pharmacy for both community and institutional practices. Students, based upon those competency standards, must achieve a passing mark on each competency stated in order to pass that practice-based course. In passing the practice-based courses, the School is essentially stating that that student is competent to sit for the board examination and practice as a competent pharmacist once the student has passed the board exam, and

WHEREAS, at this point in time, only a small contingent of those graduating seek positions in the pharmaceutical and managed care industries (perhaps less than 10% of the graduating students), their role in being versed in good patient care principles and standards of care is not diminished based upon the demands of these entities both directly and indirectly being responsible for the assurance that the highest of standards be undertaken that all services and/or products rendered or produced shall be of the highest quality to the recipients of those services and/or products, and

WHEREAS it has not been established, as to at least the knowledge of those who have created this resolution and recommendation, that 1500 hours of patient-related contact is either over or under abundant in assuring that a pharmacist will be minimally competent to practice patient-care pharmacy upon being licensed,

THEREFORE LET IT BE RESOLVED/RECOMMENDED that the California State Board of Pharmacy (Board) recognize that intern experiences in the areas of pharmaceutical industry and managed care can have both a direct and indirect impact on patient care. In so recognizing, be it resolved and recommended that the Board allocate up to 400 hours from the 900 hour remainder that does not include the 600 hours allocated to pharmacy school experiential programming for the purposes of gaining experience in new pharmacy practice related areas such as and not limited to industrial pharmacy and managed care.

THEREFORE LET IT FURTHER BE RESOLVED/RECOMMENDED as a modification of *Title 16, Calif. Code of Regulations, Section 1718[a][1][A-D]* that presently reads as follows:

- (a) *Prior to receiving authorization from the board to take the pharmacist licensure examinations required by section 4200 of the Business and Professions Code, applicants shall submit to the board the following:*
 - (1) *Proof of 1500 hours of pharmacy practice experience that meets the following requirements:*
 - (A) *A minimum of 900 hours of pharmacy practice experience obtained in a pharmacy.*
 - (B) *A maximum of 600 hours of pharmacy practice experience may be granted at the discretion of the board for other experience substantially related to the practice of pharmacy.*
 - (C) *Experience in both community pharmacy and institutional pharmacy practice settings.*
 - (D) *Pharmacy practice experience that satisfies the requirements for both introductory and advanced pharmacy practice experiences established by the Accreditation Council for Pharmacy Education.*

THAT THE MODIFICATION OF *Title 16, Calif. Code of Regulations, Section 1718[a][1][A-D]* BE AS FOLLOWS:

- (a) *Prior to receiving authorization from the board to take the pharmacist licensure examinations required by section 4200 of the Business and Professions Code, applicants shall submit to the board the following:*
 - (1) *Proof of 1500 hours of pharmacy practice experience that meets the following requirements:*
 - (A) *A minimum of 500 hours of pharmacy practice experience must be obtained in community and institutional pharmacy practice settings.*
 - (B) *A maximum of 1000 hours of pharmacy-related practice experience must be obtained under the supervision of a pharmacist. This 1000 hours may involve, but is not limited to the attainment of pharmacy-related practice experience in a community pharmacy, an institutional pharmacy setting, a managed care organization, and a pharmaceutical industrial setting. The 1000 hours shall include the current 600 hours that is granted for pharmacy school experiential programming, and the additional 400 hours for other pharmacist supervised pharmacy-related experiences.*
 - (C) *Pharmacy practice experience that satisfies the requirements for both introductory and advanced pharmacy practice experiences established by the Accreditation Council for Pharmacy Education.*



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03/14/2006 03:12 PM

Dear Patricia,

Thank you for sending the agenda for the March 22nd meeting. We would like to present during the first agenda item. I will be accompanied by my colleague Kimberly Bardel Whitlock, Pharm.D., also a clinical pharmacist with the National Oncology Alliance.

Please find attached supporting documents for our presentation. We would also like to provide our treatment guideline on larger 11 x 17 paper for ease of use. How many copies do you suggest we bring?

Thank you again, please let me know if there is anything further we need to do in preparation for March 22nd.

Cindy

Cynthia G. Baker, Pharm.D.
Manager, Clinical Services
National Oncology Alliance, Inc.
750 Lindaro St., Suite 350, San Rafael, CA 94901
www.noainc.com
Direct: 415.526.8137 Fax: 415.482.1683
Executive Assistant: Jennifer Boss 415.526.8162
National Oncology Alliance (NOA) provides essential clinical and business information, resources and insight to help transform the practice of oncology.

-----Original Message-----
From: Patricia_Harris@dca.ca.gov
[mailto:Patricia_Harris@dca.ca.gov]
Sent: Friday, March 10, 2006 5:04 PM
To: Cindy Baker
Subject: Licensing Committee Meeting

Attached is the agenda for the March 22nd meeting.

(See attached file: LicComMar06Agenda.doc)



- NOA Rx Intern Job Description 2-2006.doc



- NOA Intern Correlation CPJE Exam Content.doc



- Breast_Guideline_NOA_guideline_v2-1_2005.pdf

National Oncology Alliance, Inc. (NOA)
 750 Lindero Street, Suite 350
 San Rafael, CA 94954
 (415) 526-8137

NOA Intern Activity Correlation with CPJE Exam Content

Job duties performed by an intern pharmacist employed with the National Oncology Alliance provide experience necessary to prepare for CPJE exam. The table below lists intern duties and the specific correlating exam content.

Please note the CPJE content is pulled directly from the content listed on the California State Board of Pharmacy website, including the same alphabetical and numerical outline format for ease of comparison.

NOA Intern Job Duties	CPJE Exam Content
<p>Assist the clinical team with development and yearly revision of the NOA Treatment Guidelines.</p> <p>These 48 evidence-based guidelines cover cancer and supportive care treatment topics, and include categories of information such as diagnostic workup, tumor staging, initial treatment, adjuvant treatment, recurrent/refractory treatment, and patient monitoring and follow up.</p> <p>Detailed information regarding regimen selection, components, dosing including frequency, duration, and administration are provided. Drug complications (i.e. adverse effects), contraindications, and patient-specific considerations in choosing drug therapy are also addressed in the guidelines.</p>	<p>Provide Medication to Patients</p> <p>A. Organize and Evaluate Information</p> <ol style="list-style-type: none"> 1. Interpret prescription/medication order 2. Obtain information from the patient/ patient's representative for patient profile (diagnosis or desired therapeutic outcome, allergies, adverse reactions, medical history, etc.) 3. Obtain information from prescriber and/or health care professionals for patient profile (diagnosis or desired therapeutic outcome, allergies, adverse reactions, medical history, etc.) 4. Assess prescription / medication order for completeness, correctness, authenticity, and legality 5. Assess prescription/medication order for appropriateness (e.g. drug selection, dosage, drug interactions, dosage form, delivery system) 6. Evaluate the medical record/patient profile for any or all of the following: disease states, clinical condition, medication use, allergies, adverse reactions, disabilities, medical/surgical therapies, laboratory findings, physical assessments, and/or diagnostic tests 7. Evaluate the pharmaceutical information needs of the patient/patient's representative <p>Monitor and Manage Patient Outcomes</p> <p>A. Determine a Course of Action and Manage Patient Outcomes</p> <ol style="list-style-type: none"> 1. Determine desired therapeutic outcomes 2. Develop a therapeutic regimen for prescription medications (e.g., recommend alteration of prescribed drug regimen; select drug if necessary) 3. Determine the need for a referral 4. Communicate the therapeutic plan to the patient/patient's representative, the prescriber and other health care professionals 5. Recommend/order necessary monitoring and screening procedures (e.g., blood pressure, glucose levels, drug levels) 6. Communicate results of monitoring to

	<p>patient/patient's representative, prescriber and/or other health care professionals</p> <p>7. Manage drug therapy according to protocols</p>
<p>Assist the clinical team with development and yearly revision of the NOA Patient Education handouts.</p> <p>This library of over 125 handouts follow the Department of Health and Human Services Keystone Guidelines in the provision of information about the uses and benefits, precautions, drug interactions, adverse effects, administration, and storage of chemotherapy and supportive care agents. The library also covers symptom management topics including management of neutropenia, anemia, peripheral neuropathy, nausea and vomiting, sexual dysfunction, sleep disturbance, and others.</p>	<p>Provide Medication to Patients</p> <p>A. Organize and Evaluate Information</p> <p>7. Evaluate the pharmaceutical information needs of the patient/patient's representative</p> <p>B. Dispense Medications</p> <p>6. Select auxillary labels(s) for container(s).</p> <p>Monitor and Manage Patient Outcomes</p> <p>A. Determine a Course of Action and Manage Patient Outcomes</p> <p>2. Communicate the therapeutic plan to the patient / patient's representative, the prescriber and other health care professionals</p> <p>B. Educate Patients and Health Care Professionals</p> <p>1. Assess the patient's understanding of the disease and treatment</p> <p>2. Counsel patient/patient's representative regarding prescription medication</p> <p>5. Counsel patient/patient's representative regarding non-drug therapy</p> <p>6. Counsel patient/patient's representative regarding self-monitoring of therapy (e.g., devices, symptoms)</p>
<p>Prepare clinical summaries of studies supporting the use of specific chemotherapy or supportive care treatment regimens.</p> <p>Summaries include a description of study design, study population, inclusion and exclusion parameters, treatment regimen(s), outcomes measures and results, monitoring requirements, reported adverse effects, and statistical analysis. Summaries are generally one page, written for use by oncologists, nurses, and pharmacists.</p>	<p>Provide Medication to Patients</p> <p>A. Organize and Evaluate Information</p> <p>1. Interpret prescription/ medication order</p> <p>2. Obtain information from the patient/ patient's representative for patient profile (diagnosis or desired therapeutic outcome, allergies, adverse reactions, medical history, etc.)</p> <p>3. Obtain information from prescriber and/or health care professionals for patient profile (diagnosis or desired therapeutic outcome, allergies, adverse reactions, medical history, etc.)</p> <p>4. Assess prescription/medication order for completeness, correctness, authenticity, and legality</p> <p>5. Assess prescription /medication order for appropriateness (e.g. drug selection, dosage, drug interactions, dosage form, delivery system)</p> <p>6. Evaluate the medical record/patient profile for any or all of the following: disease states, clinical condition, medication use, allergies, adverse reactions, disabilities, medical/surgical therapies, laboratory findings, physical assessments, and/or diagnostic tests</p> <p>7. Evaluate the pharmaceutical information needs of the patient/patient's representative</p> <p>Monitor and Manage Patient Outcomes</p> <p>A. Determine a Course of Action and Manage Patient</p>

	<p>Outcomes</p> <ol style="list-style-type: none"> 1. Determine desired therapeutic outcomes 2. Develop a therapeutic regimen for prescription medications (e.g., recommend alteration of prescribed drug regimen; select drug if necessary) 3. Determine the need for a referral 4. Communicate the therapeutic plan to the patient/patient's representative, the prescriber and other health care professionals 5. Recommend/order necessary monitoring and screening procedures (e.g., blood pressure, glucose levels, drug levels) 6. Communicate results of monitoring to patient/patient's representative, prescriber and/or other health care professionals 7. Manage drug therapy according to protocols
<p>Enter, review, or modify content in the web-based NOA Compare clinical and cost/reimbursement analysis tool with the guidance of the clinical staff.</p> <p>Information the intern will enter/review/modify includes drug therapy regimen components, dosing, administration (including associated premedications, vehicles, and antiemetics), reported adverse effects, and recommended monitoring parameters[CB1][CB2] (e.g. laboratory tests).</p>	<p>Provide Medication to Patients</p> <ol style="list-style-type: none"> A. Organize and Evaluate Information <ol style="list-style-type: none"> 1. Interpret prescription/medication order 2. Obtain information from the patient/ patient's representative for patient profile (diagnosis or desired therapeutic outcome, allergies, adverse reactions, medical history, etc.) 3. Obtain information from prescriber and/or health care professionals for patient profile (diagnosis or desired therapeutic outcome, allergies, adverse reactions, medical history, etc.) 4. Assess prescription / medication order for completeness, correctness, authenticity, and legality 5. Assess prescription /medication order for appropriateness (e.g. drug selection, dosage, drug interactions, dosage form, delivery system) 6. Evaluate the medical record/patient profile for any or all of the following: disease states, clinical condition, medication use, allergies, adverse reactions, disabilities, medical/surgical therapies, laboratory findings, physical assessments, and/or diagnostic tests 7. Evaluate the pharmaceutical information needs of the patient/patient's representative <p>Monitor and Manage Patient Outcomes</p> <ol style="list-style-type: none"> A. Determine a Course of Action and Manage Patient Outcomes <ol style="list-style-type: none"> 1. Determine desired therapeutic outcomes 2. Develop a therapeutic regimen for prescription medications (e.g., recommend alteration of prescribed drug regimen; select drug if necessary) 3. Determine the need for a referral 4. Communicate the therapeutic plan to the patient/patient's representative, the prescriber and other health care professionals 5. Recommend/order necessary monitoring and screening procedures (e.g., blood pressure, glucose levels, drug levels)

	<p>6. Communicate results of monitoring to patient/patient's representative, prescriber and/or other health care professionals</p> <p>7. Manage drug therapy according to protocols</p>
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BREAST CANCER, FEMALE HIGH-RISK ASSESSMENT

Diagnostic Work-Up

High-Risk Breast Assessment

- Mammogram
- Obtain family history and assess the need for and the appropriateness of genetic counseling/testing.
- Assess patient for overall risk according to the Gall Model for Risk Assessment. Risk factors include the following. Refer to the NCI website for further information.
 - current age
 - age at menarche
 - age at first live birth
 - number of previous breast biopsies
 - presence of atypical hyperplasia
 - number of first degree relatives
- History and physical exam

Emerging Issues:

- Nipple aspirate and ductal lavage for purposes of risk stratification remain investigational at this time
- MRI breast screening may be used in very high risk patients such as BRCA-1 and -2 mutation carriers and women with very dense breasts as small studies have shown it to be more sensitive than mammography.

Staging

High-Risk Breast Assessment

No diagnosis of cancer but strong family history or BRCA-1/ BRCA-2 positive

Risk Reduction Intervention

High-Risk Breast Assessment

- For patients with BRCA-1 and/or -2 mutations consider:
- Lifestyle modification
 - Tamoxifen 20 mg PO QD x 5 years after discussion of pros and cons
 - Clinical trials - Please refer to the following website for available clinical trials: <http://cancertrials.nci.nih.gov/>

Initial Treatment

High-Risk Breast Assessment

- Appropriate genetic testing and counseling
- Discuss pros and cons of prophylactic mastectomy and/or prophylactic oophorectomy
- Clinical trials in cancer prevention - Please refer to the following website: <http://cancertrials.nci.nih.gov/>

Adjuvant Treatment

High-Risk Breast Assessment

Not Applicable

First and Subsequent Recurrent/Refractory Treatment

High-Risk Breast Assessment

Not Applicable

Monitoring/Follow-Up

High-Risk Breast Assessment

- History & physical exam every 6-12 months
- Annual mammogram if prophylactic mastectomy not chosen
- Monitor for ovarian cancer if prophylactic oophorectomy not chosen. This typically includes the following every 6-12 months:
 - Transvaginal ultrasound
 - CA-125

Emerging Issue

MRI breast screening may be used in very high risk patients such as BRCA-1 and -2 mutation carriers and women with very dense breasts as small studies have shown it to be more sensitive than mammography. Some clinicians may do this procedure annually or may alternate every 6 - 12 months the MRI with the mammogram.

Expert Panel:

Debu Tripathy, MD: Director, Komen Center for Breast Cancer Research University of Texas Southwestern Medical Center at Dallas
 Marilyn Leitch, MD: University of Texas Southwestern Medical Center at Dallas
 Linda Bosseman, MD: Wilshire Oncology Medical Group in Rancho Cucamonga, CA

BREAST CANCER, FEMALE Stage 0

Diagnostic Work-Up

Stage 0: LCIS

To make the diagnosis obtain the following:

- Bilateral mammography
- biopsy of lesion (core, incisional or excisional)

Initial work up consists of the following:

- Review pathology results
 - Obtain family history and assess the need for and the appropriateness of genetic counseling/testing
 - Assess patient for overall risk according to the Gail Model for Risk Assessment.
- Risk factors include the following. Refer to the NCI website for further information.
- current age
 - age at menarche
 - age at first live birth
 - number of previous breast biopsies
 - presence of atypical hyperplasia
 - number of first degree relatives
- History and physical exam

Emerging Issues:

- Nipple aspirate and ductal lavage for purposes of risk stratification *remain investigational at this time*

Staging

Stage 0: LCIS -

5yr survival: 98%

Tis, NO, MO
(25% chance of developing an invasive cancer in either breast within 25 years)

Tis: Carcinoma in situ, intraductal carcinoma, lobular carcinoma in situ, or Paget's disease of the nipple with no associated tumor mass

NO: No regional lymph node metastasis
MO: No distant metastasis

Stage 0: LCIS -

- Consider lifestyle modification
- Consider tamoxifen 20 mg PO QD x 5 years after discussion of pros and cons
- Clinical trials - Please refer to the following website for available clinical trials: <http://cancertrials.nci.nih.gov/>

Initial Treatment

Stage 0: LCIS

Patients may be considered for:

- Close surveillance is strongly recommended
- Bilateral simple mastectomy/reconstruction (consider in women with a strong family history)
- Clinical trials in cancer prevention - Please refer to the following website: <http://cancertrials.nci.nih.gov/>

Stage 0: LCIS

None

First and Subsequent Recurrent/Refractory Treatment

Stage 0: LCIS

If patient develops local or invasive disease, restage and treat according to stage.

Stage 0: LCIS

- History & physical exam every 6 - 12 months
- Annual mammogram
- Patients receiving tamoxifen should have a yearly gynecologic exam (if no prior hysterectomy) and should be carefully questioned regarding vaginal discharge or bleeding.

Monitoring/Follow-Up

Stage 0: DCIS

To make the diagnosis obtain the following:

- Bilateral mammography
- biopsy of lesion (core, incisional or excisional)

Initial work up consists of the following:

- Review pathology results
 - Obtain family history and assess the need for and the appropriateness of genetic counseling/testing
 - Assess patient for overall risk according to the Gail Model for Risk Assessment.
- Risk factors include the following. Refer to the NCI website for further information.
- current age
 - age at menarche
 - age at first live birth
 - number of previous breast biopsies
 - presence of atypical hyperplasia
 - number of first degree relatives
- History and physical exam

Stage 0: DCIS:

5yr survival: 98%

Tis, NO, MO

Tis: Carcinoma in situ, intraductal carcinoma, lobular carcinoma in situ, or Paget's disease of the nipple with no associated tumor mass

NO: No regional lymph node metastasis
MO: No distant metastasis

Stage 0: DCIS

- Consider lifestyle modification
- Consider Tamoxifen 20 mg PO QD x 5 years after discussion of pros and cons
- Clinical trials - Please refer to the following website for available clinical trials: <http://cancertrials.nci.nih.gov/>

Stage 0 - DCIS

Patients may be considered for mastectomy or wide excision. The treatment choice depends upon tumor characteristics and the patient's desire for breast preservation. The survival benefit is equivalent for the following options if the DCIS can be completely resected:

- Excision alone with wide negative margins (*ideally ≥ 1cm*) for small, low grade tumors
- Specimen radiographs should be done to ensure removal of density and/or calcifications
- Excision with negative margins plus radiation for high grade tumors
- Simple mastectomy which may be followed by immediate or delayed reconstruction
- Clinical trials - Please refer to the following website for available clinical trials: <http://cancertrials.nci.nih.gov/>

Notes:

- Axillary node dissection is generally not indicated for DCIS
- *When a mastectomy is done, SLND should be strongly considered as invasive disease may be found in the mastectomy final pathology exam. If the breast has been removed, SLND cannot be performed and ALND would be required for axillary staging.*
- *If breast conserving surgery is performed for high risk DCIS, SLND may be done.*

Note: After excision of mammographically detected DCIS with microcalcifications, obtain a follow-up mammogram if breast preservation chosen.

Stage 0 - DCIS

- Radiation depending on grade, size and margins
- Tamoxifen 20 mg PO QD x 5 years in hormone-receptor positive patients who have undergone breast conserving surgery and radiation
- *The efficacy of tamoxifen without radiation in preventing local recurrence has not been established*

Stage 0 - DCIS

The options for recurrent disease therapy include:

- Re-excision followed by radiation (if no prior radiation)
- Simple mastectomy which may be followed by immediate or delayed reconstruction
- If patient has invasive disease, restage and treat according to stage

Stage 0 - DCIS

- History & Physical Exam every 6 months
- Mammography every 6 months x 1 year then annually thereafter
- Patients receiving tamoxifen should have a yearly gynecologic exam (if no prior hysterectomy) and should be carefully questioned regarding vaginal discharge or bleeding.

BREAST CANCER, FEMALE Stage I

Diagnostic Work-up

Stage I:

- To Make the Diagnosis:
- bilateral mammography
 - biopsy of lesion (core, incisional or excisional)

Initial Work-up Consists of the Following:

- History and physical exam
- CBC, Pts & Diff., Chemistry panel
- Chest X-ray if clinically indicated
- Review pathology results
- Scans as clinically indicated
- **Baseline** MUGA scan or Echo if clinically indicated for patients receiving anthracycline or trastuzumab
- Evaluate the following prognostic factors:
 - tumor size and grade
 - lymph node involvement
 - age/ menopausal status
 - ER/PR status
 - S-phase may be used to assist in decision making
 - **HER-2/neu status should be obtained for future use if patient were to relapse but remains controversial for guidance in decision making for early-stage disease**

Note: The likelihood of metastatic disease detected by radiographic means in an asymptomatic individual needs to be weighed against the chance of a false positive and the evaluation that would ensue. Routine bone scans in patients with stage I/II disease could be reserved for those with musculoskeletal symptoms or elevated alkaline phosphatase.

Emerging Issues:

- At this time, the optimal method of testing HER 2/neu over expression (immunohistochemistry vs. FISH) remains undefined. Some experts agree that if HER-2/neu by immunohistochemistry is 0, 1+, or 2+, the results are reliable. However, if 2+, they recommend sending for FISH. Testing should be performed at experienced testing centers.
- A new 21-gene assay has shown a high degree of accuracy in predicting recurrence risk and benefit from chemotherapy in patients with node-negative, ER+ breast cancer, however, more validation is in progress. To date, the use of these assays has not been demonstrated to lead to a better outcome than conventional staging and grading.

Staging

Stage I:

5yr survival: 90%
T1, N0, M0

Initial Treatment

Stage I:

- Treatment approach depends upon tumor characteristics, breast size and patient's desire to preserve the breast. **Assessment of axillary lymph node status for clinically node negative patients is recommended by way of a sentinel lymph node dissection, if SLND is unavailable, an axillary lymph node dissection may be done**

Note: Quality standards for sentinel lymph node dissection have been set by the ACOSOG and ASBS. Standards include 30 cases where sentinel lymph node has been identified followed by complete dissection with 85% sentinel lymph node identification with 95% specificity.

- For patients in whom chemotherapy is not a consideration (e.g. elderly patients with very favorable tumors), the elimination of axillary lymph node dissection may be considered.

The survival benefit is equivalent for the following 2 options:

- Lumpectomy followed by whole breast radiation. Following excision, the margins should be evaluated.
 - if positive margins are observed, a more extensive excision should be performed.
 - if negative margins are not possible, a mastectomy should be performed.
- Modified radical mastectomy or simple mastectomy which may be followed by immediate or delayed reconstruction. Patients with positive margins should receive chest wall radiation.

Clinical trials - Please refer to the following website for available clinical trials: <http://cancerwfs.ncl.nih.gov/>

Emerging Issues:

Partial breast radiation is being done. Studies to date have reported low recurrence rates in patients of low risk for local recurrence. A prospective trial is currently underway which may help define the risks and benefits of this approach.

Adjuvant Treatment

Stage I:

All tumors < 1 cm independent of other factors:

(Note: there have not been adequately sized studies in this population of patients to support specific evidence-based treatment recommendations)

- No Treatment
- Follow treatment recommendations below based upon hormone receptor status, menopausal status, and other patient specific factors

Hormone receptor positive, pre-menopausal (tumor > 1cm)

There are multiple different ways in which hormonal therapy and chemotherapy may be combined. Treatment options include combining 1 or more selections from the hormone column with 1 selection from the chemotherapy column. When chemotherapy and hormonal therapy are both used they should be given sequentially.

Chemotherapy†‡	Hormonal Therapy
<ul style="list-style-type: none"> • None • CMF x 6 cycles or 8 cycles depending on regimen used • AC x 4 cycles • CAF/FAC x 6 cycles • FEC/CEF x 6 cycles • AC → Paclitaxel or Docetaxel • Dose Dense AC → Paclitaxel • TAC 	<ul style="list-style-type: none"> • Tamoxifen x 5 years. When patients become menopausal, an aromatase inhibitor should be added for 5 years. • LHRH Agonist (Goserelin, Leuprolide) • Oophorectomy <p>Note: In women who are recently rendered post-menopausal, ovarian estrogen production may persist therefore estradiol levels with high sensitivity assay should be done to confirm menopausal status. A level of < 10 picograms/dL should be observed.</p>

Hormone Receptor positive, postmenopausal (tumor > 1cm)

There are multiple different ways in which hormonal therapy and chemotherapy may be combined. Treatment options include combining 1 or more selections from the hormone column with 1 selection from the chemotherapy column. When chemotherapy and hormonal therapy are both used they should be given sequentially and not concurrently

Chemotherapy†‡	Hormonal Therapy
<ul style="list-style-type: none"> • None • CMF x 6 cycles or 8 cycles depending on regimen used • AC x 4 cycles • CAF/FAC x 6 cycles • FEC/CEF x 6 cycles • AC → Paclitaxel or Docetaxel • Dose Dense AC → Paclitaxel • TAC 	<ul style="list-style-type: none"> • Aromatase inhibitor (AI) x 5 years • Tamoxifen x 2 yrs followed by an AI x 3 yrs • Tamoxifen x 5 years • Tamoxifen x 5 yrs followed by an AI x 5 yrs <p>Note: No benefit has been seen with continuation of tamoxifen longer than 5 yrs. The overall survival benefit of using an AI instead of or following tamoxifen has not yet been demonstrated. The use of an AI in place of or after 2 yrs. of tamoxifen has demonstrated a significant benefit on recurrence-free survival during the first 10 years after diagnosis.</p> <p>Note: In women who are recently rendered post-menopausal, ovarian estrogen production may persist therefore estradiol levels with high sensitivity assay should be done to confirm menopausal status. A level of < 10 picograms/dL should be observed.</p>

Hormone Receptor negative, pre- and postmenopausal (tumor > 1cm) - high risk node negative disease

Hormone therapy in this group of patients is not appropriate. Choose a treatment option from the chemotherapy column.

Chemotherapy†‡	Hormonal Therapy
<ul style="list-style-type: none"> • None • CMF x 6 cycles or 8 cycles depending on regimen used • AC x 4 cycles • CAF/FAC x 6 cycles • FEC/CEF x 6 cycles • AC → Paclitaxel or Docetaxel • AC → Paclitaxel + Trastuzumab (for HER2+ patients only) • Dose Dense AC → Paclitaxel • TAC 	<ul style="list-style-type: none"> • None

† The more intensive chemotherapy regimens are accompanied by greater toxicity and cost and must be balanced by the patient's overall risk and absolute benefit. Higher risk tumors based on size, grade, lymphovascular invasion and other aggregated characteristics may warrant more aggressive chemotherapy regimens.

‡ There are inadequate data to draw conclusions about the benefit of chemotherapy in women > 70 yrs. For all other age groups there is evidence of benefit. Benefit from chemotherapy is greater in younger women and steadily decreases with age.

Emerging Issues:

- Choosing an AI over tamoxifen based on HER-2/neu protein overexpression is currently under study and should not affect treatment decisions at this time.

Monitoring/Follow-Up

Stage I

- History/Physical Exam
 - every 6 months years 1-3 after primary therapy, then every 6-12 months years 4-5, then annually thereafter
- Follow-up of the patient should be coordinated and not duplicated. Continuity of care should be conducted by a physician experienced in the surveillance of cancer patients.
- Annual mammogram
- Blood work, chest X-ray and scans if clinically indicated
- Patients receiving tamoxifen should have a yearly gynecologic exam (if no prior hysterectomy) and should be carefully questioned regarding vaginal discharge or bleeding.
- Patients receiving an aromatase inhibitor should have periodic monitoring of bone mineral density. Anti-resorptive therapy (preferable a non-SERM) should be considered if bone mineral density is depressed and all patients should take calcium and vitamin D
- The use of serum markers for following response in patients with recurrent disease should be restricted to patients in whom other objective measures are equivocal
- In women who are recently rendered postmenopausal, ovarian estrogen production may persist therefore estradiol levels with high sensitivity assay should be done to confirm menopausal status. A level of < 10 picograms/dL should be observed.
- Patients with BRCA-1 and 2 mutations that have not elected to undergo contralateral prophylactic mastectomy, consider annual MRI screening
- Patients receiving trastuzumab should have cardiac monitoring at 3, 6, and 12 months after beginning trastuzumab therapy. Trastuzumab therapy should be withheld for the following:
 - > if ejection fraction drops more than 10% below the institutional normal
 - > if the EF drops more than 15% overall
 - > Clinical CHF with a documented drop in EF
 - > If EF normalizes within 4 weeks may consider resuming trastuzumab therapy

BREAST CANCER, FEMALE Stage II-IIIA

Diagnostic Work-Up

- Stage II - IIIA**
- History and physical exam
 - CBC, Pts & Diff., Chem panel
 - bilateral mammography
 - biopsy of lesion (core, incisional or excisional)

- Initial Work-up consists of the following:
- History and physical exam
 - CBC, Pts & Diff., Chem panel
 - Chest X-ray if clinically indicated
 - Review pathology results
 - Scans as clinically indicated
 - Baseline MUGA scan or Echo if clinically indicated for patients receiving anthracycline or herceptin
- Evaluate the following prognostic factors:
- tumor size and grade
 - S-phase may be used to assist in decision making
 - ER/PR levels
 - lymph node involvement
 - menopausal status
 - **HER-2/neu status should be obtained for future use if patient were to relapse but remains controversial for guidance in decision making for early-stage disease**

Note: The likelihood of metastatic disease detected by radiographic means in an asymptomatic individual needs to be weighed against the chance of a false positive and the evaluation that would ensue. Routine bone scans in patients with stage III disease could be reserved for those with musculoskeletal symptoms or elevated alkaline phosphatase.

Emerging Issues:

At this time, the optimal method of testing HER-2/neu over-expression (immunohistochemistry vs. FISH) remains undefined. Some experts agree that if HER-2/neu by immunohistochemistry is 0, 1+, or 3+, the results are reliable. However, if 2+, they recommend sending for FISH. Testing should be performed at experienced testing centers.

Staging

Stage II - III:
5yr survival: 75%

Stage IIA
T0, N1, M0
T1, N1, M0
T2, N0, M0

Stage IIB
T2, N1, M0
T3, N0, M0

Initial Treatment

Stage II-IIIa

Treatment approach depends upon tumor characteristics, breast size and patient's desire to preserve the breast. **Assessment of axillary lymph node status for clinically node negative patients is recommended by way of a sentinel lymph node dissection. If SLND is unavailable, an axillary lymph node dissection may be done.**

- Neoadjuvant chemotherapy may be considered for patients who would benefit from cytoreduction and in whom chemotherapy will be part of their treatment regimen. Patients should continue to receive chemotherapy until the complete neoadjuvant regimen is given, until response plateau achieved, or until progression. If the patient progresses during chemotherapy, change the regimen, perform a modified radical mastectomy, or breast conserving surgery, if feasible. The objective response to chemotherapy should be assessed with each cycle. Regimens which may be considered for neoadjuvant administration include:
 - Anthracycline-based regimen (AC, FAC, CAF, FEC, CEF) or AC followed by a taxane.
 - > **HER2 positive patients may be considered for anthracycline-based therapy followed by a combination of trastuzumab plus paclitaxel**
 - Docetaxel - Capecitabine
 - Doxorubicin - Paclitaxel
 - CMF
 - Tamoxifen alone can be considered in post-menopausal hormone receptor positive women and should be added after chemotherapy for pre-menopausal woman.
 - > If tumor reduction is not suitable for breast conserving surgery, consider modified radical mastectomy and axillary node dissection if SLND not done followed by external beam radiation to the breast and nodal regions. The use of SLND following neoadjuvant chemotherapy can be considered.
 - > If tumor size is significantly decreased, consider conservative treatment (e.g., quadrantectomy) and axillary node dissection (if SLND not done) followed by external beam radiation to the breast and nodal region. The use of SLND following neoadjuvant chemotherapy can be considered.

- Lumpectomy followed by radiation if tumor is ≤ 5 cm. Following excision, the margins should be evaluated.
 - If positive margins are observed, a more extensive excision should be performed.
 - If negative margins are not possible, a mastectomy should be performed.

- Modified radical mastectomy or simple mastectomy (in women with a negative SLND or in those who have already had an axillary lymph node dissection) which may be followed by immediate or delayed reconstruction.
 - Patients with positive margins or who have ≥ 4 positive lymph nodes should receive radiation to the chest wall and draining lymph nodes.
 - Consider radiation for Stage II, T₂ tumors.
 - Radiotherapy may be considered for patients with 1-3 positive nodes particularly if unfavorable tumor characteristics.
 - Radiation generally follows chemotherapy.

- Clinical trials - Please refer to the following website for available clinical trials: <http://cancertrials.nci.nih.gov/>

Emerging Issues:

The use of trastuzumab in the neoadjuvant setting for HER-2/neu positive operable breast cancer was associated with a higher pathological complete response rate in one small randomized trial, but has not yet been shown to improve long-term outcome, hence this remains investigational.

Adjuvant Treatment

Stage II - IIIA

- All patients who have not received neoadjuvant therapy should receive adjuvant systemic therapy. For patients who have received neoadjuvant chemotherapy, additional chemotherapy after surgery may be considered. Patients with > 10 positive nodes are considered high-risk for relapse. Anthracycline-based chemotherapy for 6 cycles or a taxane containing regimen is the preferred adjuvant therapy.
- For patients that are HER2 positive who have already completed adjuvant chemotherapy, consideration can be given to administering a year of trastuzumab therapy

Hormone receptor positive, premenopausal (tumor > 1cm):

There are multiple different ways in which hormonal therapy and chemotherapy may be combined. Treatment options include combining 1 or more selections from the hormone column with 1 selection from the chemotherapy column. When chemotherapy and hormonal therapy are both used they should be given sequentially.

Chemotherapy †‡	Hormonal Therapy
<ul style="list-style-type: none"> • None • CMF x 6 cycles or 8 cycles depending on regimen used • AC x 4 cycles • Epirubicin - tamoxifen (elderly) 	<ul style="list-style-type: none"> • Tamoxifen x 5 years. When patients become menopausal, an aromatase inhibitor should be added for 5 years • LHRH Agonist (Goserelin, Leuprolide) • Oophorectomy
<ul style="list-style-type: none"> • CAF/FAC x 6 cycles • FEC/CEF x 6 cycles • AC -> Paclitaxel or Docetaxel • FEC-100 x 3 -> Docetaxel x 3 • AC -> Paclitaxel + Trastuzumab (for HER2 + patients only) • Dose Dense AC -> Paclitaxel • TAC 	<p>Note: In women who are recently rendered postmenopausal, ovarian estrogen production may persist therefore estradiol levels with high sensitivity assay should be done to confirm menopausal status. A level of < 10 picograms/dL should be observed.</p>

Hormone Receptor positive, postmenopausal (tumor > 1cm)

There are multiple different ways in which hormonal therapy and chemotherapy may be combined. Treatment options include combining 1 or more selections from the hormone column with 1 selection from the chemotherapy column. When chemotherapy and hormonal therapy are both used they should be given sequentially and not concurrently.

Chemotherapy †‡	Hormonal Therapy
<ul style="list-style-type: none"> • None • CMF x 6 cycles or 8 cycles depending on regimen used • AC x 4 cycles • Epirubicin - tamoxifen (elderly) 	<ul style="list-style-type: none"> • Aromatase Inhibitor (AI) x 5 years • Tamoxifen x 2 yrs followed by an AI x 3 yrs • Tamoxifen x 5 years • Tamoxifen x 5 yrs followed by an AI x 5 yrs <p>Note: No benefit has been seen with continuation of tamoxifen longer than 5 yrs. The overall survival benefit of using an AI instead of or following tamoxifen has not yet been demonstrated. The use of an AI in place of or after 2 yrs. of tamoxifen has demonstrated a significant benefit on recurrence-free survival during the first 10 years after diagnosis.</p>
<ul style="list-style-type: none"> • CAF/FAC x 6 cycles • FEC/CEF x 6 cycles • AC -> Paclitaxel or Docetaxel • FEC-100 x 3 -> Docetaxel x 3 • AC -> Paclitaxel + Trastuzumab (for HER2 + patients only) • Dose Dense AC -> Paclitaxel • TAC 	<p>In women who are recently rendered post-menopausal, ovarian estrogen production may persist therefore estradiol levels with high sensitivity assay should be done to confirm menopausal status. A level of < 10 picograms/dL should be observed.</p>

Hormone Receptor negative pre- and postmenopausal (tumor > 1cm)

Hormone therapy in this group of patients is not appropriate. Choose a treatment option from the chemotherapy column.

Chemotherapy †‡	Hormonal Therapy
<ul style="list-style-type: none"> • None • CMF x 6 cycles or 8 cycles depending on regimen used • AC x 4 cycles 	<ul style="list-style-type: none"> • None
<ul style="list-style-type: none"> • CAF/FAC x 6 cycles • FEC/CEF x 6 cycles • AC -> Paclitaxel or Docetaxel • FEC-100 x 3 -> Docetaxel x 3 • AC -> Paclitaxel + Trastuzumab (for HER2 + patients only) • Dose Dense AC -> Paclitaxel • TAC 	

† The more aggressive chemotherapy regimens are accompanied by greater toxicity and cost and must be balanced by the patient's overall risk and absolute benefit. Higher risk tumors based on size, grade, lymphovascular invasion and other aggregated characteristics may warrant more aggressive chemotherapy regimens.

‡ There are inadequate data to draw conclusions about the benefit of chemotherapy in women > 70 yrs. For all other age groups there is evidence of benefit. Benefit from chemotherapy is greater in younger women and steadily decreases with age.

Emerging Issues:

Choosing an AI over tamoxifen based on HER-2/neu protein overexpression is currently under study and should not affect treatment decisions at this time.

Monitoring/Follow-Up

Stage II-IIIa

- History/Physical Exam
 - every 3-6 months years 1-3 after primary therapy, then every 6-12 months years 4-5, then annually thereafter
- Follow-up of the patient should be coordinated and not duplicated. Continuity of care should be conducted by a physician experienced in the surveillance of cancer patients.
- Annual mammogram
- Blood work, chest X-ray and scans if clinically indicated.
- Patients receiving tamoxifen should have a yearly gynecologic exam (if no prior hysterectomy) and should be carefully questioned regarding vaginal discharge or bleeding.
- Patients receiving an aromatase inhibitor should have periodic monitoring of bone mineral density. Anti-osteoporotic therapy (preferably a non-SERM) should be considered if bone mineral density is depressed, and all patients should take calcium and vitamin D
- The use of serum markers for following response in patients with recurrent disease should be restricted to patients in whom other objective measures are equivocal.
- In women who are recently rendered postmenopausal, ovarian estrogen production may persist therefore estradiol levels with high sensitivity assay should be done to confirm menopausal status. A level of < 10 picograms/dL should be observed.
- Patients with BRCA-1 and 2 mutations that have not elected to undergo contralateral prophylactic mastectomy, consider annual MRI screening
- Patients receiving trastuzumab should have cardiac monitoring at 3, 6, and 12 months after beginning trastuzumab therapy. Trastuzumab therapy should be withheld for the following:
 - > if ejection fraction drops more than 10% below the institutional normal
 - > if the EF drops more than 15% overall
 - > Clinical CHF with a documented drop in EF
 - > If EF normalizes within 4 weeks may consider resuming trastuzumab therapy

BREAST CANCER, FEMALE Stage IIIB/IIIC

Diagnostic Work-up

Stage IIIB/IIIC

- To make the diagnosis:
- bilateral mammography
 - biopsy of lesion (core, incisional or excisional)
 - Skin biopsy may be needed to confirm inflammatory cancer if clinical features are equivocal and pathology shows tumor cells in intradermal lymphatics.

Initial Work-up

- Consists of the following:
- History and physical exam
 - CBC, Pts & Diff., Chem panel
 - Review pathology results
 - Bone scan
 - CXR
 - Additional scans as clinically indicated (such as an abdominal CT scan if LFT's are elevated).
 - Baseline MUGA scan or Echo if clinically indicated for patients receiving anthracycline or trastuzumab
 - Evaluate the following prognostic factors:
 - tumor size and grade
 - S-phase may be used to assist in decision making
 - ER/PR levels
 - lymph node involvement
 - menopausal status
 - HER-2/neu status should be obtained for future use if patient were to relapse but remains controversial for guidance in decision making for early-stage disease

Emerging Issues:
 At this time, the optimal method of testing HER 2/neu over-expression (immunohistochemistry vs. FISH) remains undefined. Some experts agree that if HER-2/neu by immunohistochemistry is 0, 1+, or 3+, the results are reliable. However, if 2+, they recommend sending for FISH. Testing should be performed at experienced testing centers.

Staging

Stage IIIB-IIIC

(Inoperable at time of diagnosis)
 T4, N0, M0
 T4, N1, M0
 T4, N2, M0
 (includes inflammatory breast cancer)

Stage IIIC
 Any T, N3, M0

Initial Treatment

Stage IIIB-IIIC

- Neoadjuvant chemotherapy may be used to attempt and shrink the tumor so that it will be amenable to resection in patients who are inoperable at the time of presentation. Patients should continue to receive chemotherapy until the complete neoadjuvant regimen has been given, until response plateau achieved or until progression. If the patient progresses during chemotherapy, change systemic therapy or perform a modified radical mastectomy. The objective response to chemotherapy should be assessed with each cycle. Regimens that may be considered include:
 - Anthracycline-based regimen (eg, FAC, CAF, FEC, or CEF) or AC followed by a taxane.
 - HER2 positive patients may be considered for anthracycline-based therapy followed by a combination of trastuzumab plus paclitaxel
 - Docetaxel – Capecitabine
 - Doxorubicin – Paclitaxel
 - CMF
 - Tamoxifen alone can be considered in postmenopausal hormone receptor positive women and should be added after chemotherapy for premenopausal women.
 - If tumor reduction is not suitable for breast conserving surgery, consider modified radical mastectomy and axillary node dissection followed by external beam radiation to the chest wall and nodal regions.
 - If tumor size is significantly decreased, consider conservative treatment (e.g., quadrantectomy) and axillary node dissection followed by external beam radiation to the breast and nodal region.
 - If neoadjuvant chemotherapy succeeds in debulking an inoperable tumor, surgical resection should be attempted.
- Patients may be considered for modified radical mastectomy initially, followed by chemotherapy and radiation.
- Sentinel node biopsy can be considered for patients with clinically negative nodes either pre or post chemotherapy, although the false negative rate in this setting has not been firmly established
- Patients with N3 disease should be considered for surgical resection and/or radiation therapy to the supraclavicular lymph nodes.
- For patients who are not surgical candidates initially, the same chemotherapy regimens which would be used in the first recurrent/refractory treatment setting may be considered.
- Clinical trials - Please refer to the following website for available clinical trials: <http://concltrials.ncl.nih.gov>

Adjuvant Treatment

Stage IIIB-IIIC

All patients who have not received neoadjuvant therapy should receive adjuvant systemic therapy. For patients who have received neoadjuvant chemotherapy, additional chemotherapy after surgery may be considered. Patients with > 10 positive nodes are considered high-risk for relapse. Anthracycline-based chemotherapy for 6 cycles or a taxane containing regimen is the preferred adjuvant therapy.

For patients that are HER2 positive who have already completed adjuvant chemotherapy, consideration can be given to administering a year of trastuzumab therapy

Hormone receptor negative, pre-menopausal (tumor > 1cm)†

There are multiple different ways in which hormonal therapy and chemotherapy may be combined. Treatment options include combining 1 or more selections from the hormone column with 1 selection from the chemotherapy column. When chemotherapy and hormonal therapy are both used they should be given sequentially.

Chemotherapy†‡	Hormonal Therapy
<ul style="list-style-type: none"> None CMF x 6 cycles or 8 cycles depending on regimen used AC x 4 cycles Epirubicin – tamoxifen (elderly) CAF/FAC x 6 cycles FEC/CEF x 6 cycles AC – Paclitaxel or Docetaxel FEC-100 x 3 – Docetaxel x 3 AC – Paclitaxel + Trastuzumab (for HER2 + patients only) Dose Dense AC – Paclitaxel TAC 	<ul style="list-style-type: none"> Tamoxifen x 5 years. When patients become menopausal, an aromatase inhibitor should be added for 5 years LHRH Agonist (Goserelin, Leuprolide) Oophorectomy <p>In women who are recently rendered postmenopausal, ovarian estrogen production may persist therefore estradiol levels with high sensitivity assay should be done to confirm menopausal status. A level of < 10 picograms/dL should be observed.</p>

Hormone Receptor positive, postmenopausal (tumor > 1cm)†

There are multiple different ways in which hormonal therapy and chemotherapy may be combined. Treatment options include combining 1 or more selections from the hormone column with 1 selection from the chemotherapy column. When chemotherapy and hormonal therapy are both used they should be given sequentially and not concurrently.

Chemotherapy†‡	Hormonal Therapy
<ul style="list-style-type: none"> None CMF x 6 cycles or 8 cycles depending on regimen used AC x 4 cycles Epirubicin – tamoxifen (elderly) CAF/FAC x 6 cycles FEC/CEF x 6 cycles AC – Paclitaxel or Docetaxel FEC – 100 x 3 – Docetaxel x 3 AC – Paclitaxel + Trastuzumab (for HER2 + patients only) Dose Dense AC – Paclitaxel TAC 	<ul style="list-style-type: none"> Aromatase Inhibitor (AI) x 5 years Tamoxifen x 2 yrs followed by an AI x 3 yrs Tamoxifen x 5 years Tamoxifen x 5 yrs followed by an AI x 5 yrs <p>Note: No benefit has been seen with continuation of tamoxifen longer than 5 yrs. The overall survival benefit of using an AI instead of or following tamoxifen has not yet been demonstrated. The use of an AI in place of or after 2 yrs. of tamoxifen has demonstrated a significant benefit on recurrence-free survival during the first 10 years after diagnosis.</p> <p>In women who are recently rendered postmenopausal, ovarian estrogen production may persist therefore estradiol levels with high sensitivity assay should be done to confirm menopausal status. A level of < 10 picograms/dL should be observed.</p>

Hormone Receptor negative, pre- and postmenopausal (tumor > 1cm)†

Hormone therapy in this group of patients is not appropriate. Choose a treatment option from the chemotherapy column.

Chemotherapy†‡	Hormonal Therapy
<ul style="list-style-type: none"> None CMF x 6 cycles or 8 cycles depending on regimen used AC x 4 cycles CAF/FAC x 6 cycles FEC/CEF x 6 cycles AC – Paclitaxel or Docetaxel FEC-100 x 3 – Docetaxel x 3 AC – Paclitaxel + Trastuzumab (for HER2 + patients only) Dose Dense AC – Paclitaxel TAC 	<ul style="list-style-type: none"> None

† The more aggressive chemotherapy regimens are accompanied by greater toxicity and cost and must be balanced by the patient's overall risk and absolute benefit. Higher risk tumors based on size, grade, lymphovascular invasion and other aggregated characteristics may warrant more aggressive chemotherapy regimens.
 ‡ There are inadequate data to draw conclusions about the benefit of chemotherapy in women > 70 yrs. For all other age groups there is evidence of benefit. Benefit from chemotherapy is greater in younger women and steadily decreases with age.

Emerging Issues:

Choosing an AI over tamoxifen based on HER-2/neu protein overexpression is currently under study and should not affect treatment decisions at this time.

Monitoring/Follow-Up

Stage IIIB-IIIC:

- History/Physical Exam
 - every 3-6 months years 1-3 after primary therapy, then every 6-12 months years 4-5; then annually thereafter
- Follow-up of the patient should be coordinated and not duplicated. Continuity of care should be conducted by a physician experienced in the surveillance of cancer patients.
- Annual mammogram
- Blood work, chest X-ray and scans if clinically indicated.
- Patients receiving tamoxifen should have a yearly gynecologic exam (if no prior hysterectomy) and should be carefully questioned regarding vaginal discharge or bleeding.
- Patients receiving an aromatase inhibitor should have periodic monitoring of bone mineral density. Anti-resorptive therapy (preferable a non-SERM) should be considered if bone mineral density is depressed and all patients should take calcium and vitamin D
- The use of serum markers for following response in patients with recurrent disease should be restricted to patients in whom other objective measures are equivocal.
- In women who are recently rendered postmenopausal, ovarian estrogen production may persist therefore estradiol levels with high sensitivity assay should be done to confirm menopausal status. A level of < 10 picograms/dL should be observed.
- Patients with BRCA-1 and 2 mutations that have not elected to undergo contralateral prophylactic mastectomy, consider annual MRI screening
- Patients receiving trastuzumab should have cardiac monitoring at 3, 6, and 12 months after beginning trastuzumab therapy. Trastuzumab therapy should be withheld for the following:
 - If ejection fraction drops more than 10% below the institutional normal
 - If the EF drops more than 15% overall
 - Clinical CHF with a documented drop in EF
 - If EF normalizes within 4 weeks may consider resuming trastuzumab therapy

Treatment of First Recurrence (Stages I – IIIC)

Local recurrence:

- Patients who experience local recurrence after lumpectomy and radiation should undergo a mastectomy. Reconsider additional systemic therapy based upon the characteristics of the recurrence and history of previous treatment.
 - Patients who experience local recurrence after a mastectomy should be surgically resected if amenable and should receive radiation to the chest wall and lymph nodes.
- Consider additional systemic therapy. Note: No prospective data exists regarding which patients should receive additional therapy; the decision to treat should be on a case by case basis. Post-menopausal patients who were initially on tamoxifen or no hormonal therapy with ER/PR+ tumors should be placed on an aromatase inhibitor for 5 years

Isolated Metastatic Recurrences

- Single isolated cranial or pulmonary metastases should be considered for surgical resection or radiosurgery [note: radiosurgery does not apply to pulmonary lesions]
- Most patients with brain metastases should receive radiation therapy
- Patients with spinal cord compression should receive palliative radiation. Surgical decompression may be considered for selected cases
- Patients with an isolated bone metastasis may be considered for palliative radiation therapy only.
- May consider intrathecal liposomal Ara-C (DepoCyt), intrathecal MTX, appropriate
- Systemic chemotherapy or palliative radiation for patients with meningeal disease.

Metastatic recurrence:

Note: Patients with metastatic breast cancer should have their HER-2/neu status assessed if it was not done at the time of primary diagnosis. The current FDA recommendation is to treat patients who are 2+ or 3+ with trastuzumab. See "Emerging Issues" regarding 2+ HER-2/neu protein overexpression.

Hormone receptor positive and bone/soft tissue recurrence only:

- For patients who have had prior anti-estrogen within the past year, strong consideration should be given to additional 2nd line hormonal therapy.
- For patients who have had no prior anti-estrogen or who are more than 1 year off of an anti-estrogen:
 - If pre-menopausal: Tamoxifen, an LHRH Agonist, an oophorectomy or combination of some
 - If post-menopausal: tamoxifen, toremifene, or an AI (depending on previous treatment)
- Clinical trials- Refer to the following website for available clinical trials: <http://cancertrials.ncl.nih.gov>

Hormone receptor positive with symptomatic visceral disease:

- Patients with extensive visceral or immediate life-threatening disease might be optimally treated with initial chemotherapy and then considered for maintenance treatment with hormone therapy. Treatment choices include one of the following:

Combination Therapy

- Anthracycline-based therapy (AC, FAC, CAF, FEC, CEF, EC)
- Doxorubicin – taxane (doxorubicin – docetaxel or doxorubicin – docetaxel)
- Capecitabine – taxane (docetaxel or paclitaxel)
- Gemcitabine – Paclitaxel
- CMF
- Carboplatin – Paclitaxel (randomized trials have not been performed with this combination)

Single Agent Therapy (numerous combinations of the following agents have been studied in phase II trials. Many have shown efficacy but none have shown benefit over single agent therapy.)

- Single-agent taxane therapy – Gemcitabine – Vinorelbine
 - Single-agent anthracycline therapy – Infusional SFU – nab – paclitaxel (Abraxane)
 - Capecitabine – liposomal doxorubicin
- Clinical trials- Refer to the following website for available clinical trials: <http://cancertrials.ncl.nih.gov>

Hormone receptor negative, pre- and postmenopausal patients:

- For patients who recur following adjuvant chemotherapy, the treatment will depend on a number of factors, including time of recurrence, previous therapy, patient symptoms, PS, and other patient specific considerations. Treatment can include combination or single-agent chemotherapy.

Combination Therapy

- Anthracycline-based therapy (AC, FAC, CAF, FEC, CEF, EC)
- Doxorubicin – taxane (doxorubicin – paclitaxel or doxorubicin – docetaxel)
- Capecitabine – taxane (docetaxel or paclitaxel)
- Gemcitabine – Paclitaxel
- CMF
- Bevacizumab – Paclitaxel
- Carboplatin – Paclitaxel (randomized trials have not been performed with this combination)

Single Agent Therapy (numerous combinations of the following agents have been studied in phase II trials. Many have shown efficacy but none have shown benefit over single agent therapy.)

- Single-agent taxane therapy – Gemcitabine – Vinorelbine
- Single-agent anthracycline therapy – Infusional SFU – nab – paclitaxel (Abraxane)
- Capecitabine – liposomal doxorubicin

- Clinical trials- Refer to the following website for available clinical trials: <http://cancertrials.ncl.nih.gov>

HER-2/neu overexpression (3+ immunohistochemical staining and/or 2+ 3+ by FISH) Patients

- Trastuzumab combinations are considered optimal first-line therapy (not for use with anthracyclines). Alternatively, trastuzumab alone can be given to patients who are unwilling or not suitable candidates for chemotherapy. Trastuzumab combinations include:

- Trastuzumab – Paclitaxel – Trastuzumab – Vinorelbine
 - Trastuzumab – Paclitaxel – Carboplatin – Trastuzumab – Capecitabine
 - Trastuzumab – Docetaxel – Trastuzumab – Gemcitabine
 - Trastuzumab – Docetaxel – Carboplatin
- Clinical trials – Refer to the following website for available clinical trials: <http://cancertrials.ncl.nih.gov>

General Considerations regarding therapy choices:

- Many chemotherapy combinations have been tested and have shown improved response rates compared to single agents. However, these combinations are generally more toxic than single agent therapy and most have shown no improvement in survival. Combination therapy over single agents should be considered in patients with good PS and in those with aggressive disease and visceral threat.
- If the patient has received prior anthracycline therapy, further anthracycline therapy may be considered if cardiac ejection fraction is normal. Additional options to consider include the use of a less toxic anthracycline (eg, epirubicin), liposomal doxorubicin, or a cardioprotectant (dexrazoxane).
- Patients with bone disease (especially those with lytic changes on x-ray) should be considered for bisphosphonate therapy in addition to chemo- or hormonal therapy. EBRT should be reserved for painful metastases or for lesions in which pathologic fractures are imminent or have already occurred. In general, bisphosphonate therapy should continue regardless of changes in a patient's chemotherapy regimen.
- Special considerations – see last page of guideline for treatment of patients with solitary metastases, spinal cord compression and other specialty situations.

Treatment of Subsequent Recurrences (Stages I – IIIC)

Prior to initiating additional salvage therapy, assess PS and goal of therapy. Patients with good PS (ECOG 0-1) who demonstrated a response to the last regimen may be considered for additional salvage therapy. It is imperative to look for evidence of response prior to initiating each cycle (eg, subjective improvement in tumor related symptoms). After initiation of therapy, it is best to administer at least 2-3 cycles prior to evaluation for response. Scans may be indicated to follow objective response.

- For patients who progress on hormone therapy but showed an initial response, another endocrine treatment should be considered. Patients with extensive visceral or immediate life threatening disease might be optimally treated with initial chemotherapy and then considered for maintenance treatment with hormone therapy. Treatment choices include one of the following:
 - if premenopausal
 - > Oophorectomy, (either surgical or medical with a GnRH analog) + tamoxifen, or megestrol acetate
 - > Aromatase inhibitor (except aminoglutethimide)
 - if postmenopausal
 - > Faslodex
 - > Megestrol acetate

Note: The suggested order of sequence is based upon side effects and response rates. Patients with HER-2/neu positive disease are less likely to respond to hormone therapy and may have a shorter duration of response.

- For patients who recur following adjuvant chemotherapy, the treatment will depend on a number of factors, including time of recurrence, previous therapy, patient symptoms, PS, and other patient specific considerations. Treatment can include combination or single-agent chemotherapy:

Combination Therapy

- > Anthracycline-based therapy
- > Doxorubicin – taxane
- > Capecitabine – taxane (docetaxel or paclitaxel)
- > Gemcitabine – Paclitaxel
- > Carboplatin – Paclitaxel (randomized trials have not been performed with this combination)
- > CMF

Single Agent Therapy (numerous combinations of the following agents have been studied in phase II trials. Many have shown efficacy but none have shown benefit over single agent therapy.)

- > Single-agent taxane therapy
- > Single-agent anthracycline therapy
- > Capecitabine
- > liposomal doxorubicin
- > Vinorelbine
- > gemcitabine
- > infusional SFU

- For patients with Her-2/neu protein overexpression (3+ immunohistochemical staining and/or FISH+) who have progressed following first-line trastuzumab – chemotherapy, it is controversial whether trastuzumab plus another chemotherapy agent should be used as opposed to using chemotherapy alone. Trastuzumab alone is FDA approved as second line after progression on chemotherapy (without trastuzumab). However, in today's clinical practice, most patients receive trastuzumab initially:

- > Trastuzumab – Paclitaxel
- > Trastuzumab – Paclitaxel – Carboplatin
- > Trastuzumab – Docetaxel
- > Trastuzumab – Docetaxel – Carboplatin
- > Trastuzumab – Vinorelbine
- > Trastuzumab – Capecitabine
- > Trastuzumab – Gemcitabine

BREAST CANCER, FEMALE Stage IV

Diagnostic Work-up	Staging	Initial Treatment	Adjuvant Treatment	Subsequent Recurrent/Refractory Treatment	Monitoring/Follow-Up
<p>Stage IV</p> <p>To make the diagnosis:</p> <ul style="list-style-type: none"> bilateral mammography biopsy of lesion (core, incisional or excisional) <p>Initial Work-up Consists of the following:</p> <ul style="list-style-type: none"> History and physical exam CBC, Pts & Diff., Chem panel Review pathology results Bone scan CCR CT scan of abdomen. Baseline MUJA scan or Echo if clinically indicated for patients receiving anthracycline or trastuzumab Check a baseline head MRI or CT scan for patients that may receive the bevacizumab – paclitaxel combination <p>Evaluate the following prognostic factors:</p> <ul style="list-style-type: none"> Disease burden ER/PR levels menopausal status HER-2/neu status (if not done at the time of the primary diagnosis). At this time, the optimal method of testing HER-2/neu overexpression (immunohistochemistry vs. FISH) remains undefined. Some experts agree that if HER-2/neu by immunohistochemistry is 0, 1+ or 3+, the results are reliable. However, if 2+, FISH testing is recommended. Testing should be performed at experienced testing centers. 	<p>Stage IV -</p> <p>5yr survival: 10%</p> <p>Any T, any N, M1</p>	<p>Local Disease</p> <ul style="list-style-type: none"> External beam radiotherapy or a hygienic mastectomy may be recommended to control local disease. Single isolated cranial or pulmonary metastases should be considered for surgical resection or radiosurgery [note: radiosurgery does not apply to pulmonary lesions] Most patients with brain metastases should receive radiation therapy Patients with spinal cord compression should receive palliative radiation. Surgical decompression may be considered for selected cases Patients with an isolated bone metastasis may be considered for palliative radiation therapy only. May consider intrathecal liposomal Ara-C (DepoCyt), intrathecal MTX, appropriate Systemic chemotherapy or palliative radiation for patients with meningeal disease. <p>Hormone Receptor Positive with bone/soft tissue disease only:</p> <ul style="list-style-type: none"> Hormone therapy can be considered (except in the event of life threatening visceral disease). Tamoxifen – aromatase inhibitors (eg, anastrozole, letrozole) Toremifene – Fulvestrant Note: (Als, letrozole & letrozole are for postmenopausal women only) oophorectomy is an option for premenopausal women GNRH analogs (premenopausal women only) Megace. <p>Hormone Receptor positive with symptomatic visceral disease:</p> <p>Patients with extensive visceral or immediate life-threatening disease might be optimally treated with initial chemotherapy and then considered for maintenance treatment with hormone therapy.</p> <p>Combination Therapy</p> <ul style="list-style-type: none"> Antihormone-based therapy (AC, FAC, CAF, FEC, CEF, EC) Doxorubicin – Taxane (doxorubicin – paclitaxel or doxorubicin – docetaxel) Capecitabine – Taxane (docetaxel or paclitaxel) Gemcitabine – Paclitaxel Bevacizumab – Paclitaxel CMF Carboplatin – Paclitaxel (randomized trials have not been performed with this combination) <p>Single Agent Therapy (numerous combinations of the following agents have been studied in phase II trials. Many have shown efficacy but none have shown benefit over single-agent therapy.)</p> <ul style="list-style-type: none"> Single-agent taxane therapy (paclitaxel or docetaxel) Single-agent anthracycline therapy (doxorubicin or epirubicin) Capecitabine Vinorelbine Gemcitabine Infusional SFU Liposomal doxorubicin mas – paclitaxel (Abraxane) <p>Note: Treatment choice will depend on a number of factors, including previous therapy, patient symptoms, performance status, and other patient specific considerations.</p> <p>Hormone receptor negative OR visceral disease should receive chemotherapy as listed above.</p> <p>High-Risk, Node Negative or microscopically involved nodes:</p> <ul style="list-style-type: none"> For patients with high-risk, node-negative disease or microscopically involved nodes (pN1m1 or pN0 [r]) consideration can be given to the use of regimens for node-positive disease. In general, the benefit is proportional to the risk so one must factor in the associated toxicities and durations of therapy. <p>Her-2/neu overexpression (3+ Immunoperoxidase staining and/or 2+, 3+ by FISH) Patients</p> <ul style="list-style-type: none"> For patients with Her-2/neu protein overexpression (3+ immunoperoxidase staining and/or FISH+) trastuzumab combinations are considered optimal first-line therapy (not for use with anthracyclines). Alternatively, trastuzumab alone can be given to patients who are unwilling or not suitable candidates for chemotherapy. <ul style="list-style-type: none"> Trastuzumab – Paclitaxel Trastuzumab – Paclitaxel – Carboplatin Trastuzumab – Docetaxel Trastuzumab – Docetaxel – Carboplatin Trastuzumab – Vinorelbine Trastuzumab – Capecitabine <p>Note: Patients with metastatic breast cancer should have their HER-2/neu status assessed if it was not done at the time of the primary diagnosis. The current FDA recommendation is to treat patients with a 2+ or 3+. See “Emerging Issues” regarding 2+ HER-2 overexpression.</p> <ul style="list-style-type: none"> Clinical trials - Please refer to the following website for available clinical trials: http://cancertrials.nci.nih.gov Best supportive care only and referral to hospice if patient has poor performance status. 	<p>Stage IV</p> <p>Clinical trials - Please refer to the following website for available clinical trials: http://cancertrials.nci.nih.gov</p>	<p>Stage IV</p> <p>Metastatic recurrence:</p> <p>Note: Patients with metastatic breast cancer should have their HER-2/neu status assessed if it was not done at the time of primary diagnosis. The current FDA recommendation is to treat patients who are 2+ or 3+ with trastuzumab. See “Emerging Issues” regarding 2+ HER-2/neu overexpression.</p> <p>Hormone receptor positive, and bone/soft tissue disease only:</p> <ul style="list-style-type: none"> For patients who have had prior anti-estrogen within the past year, strong consideration should be given to additional 2nd line hormonal therapy. For patients who have had no prior anti-estrogen or who are more than 1 year off of an anti-estrogen: <ul style="list-style-type: none"> If pre-menopausal: Tamoxifen, an LHRH Agonist, an oophorectomy or combination of some of these If post-menopausal: tamoxifen, toremifene, or an AI (depending on previous treatment) Clinical trials - Please refer to the following website for available clinical trials: http://cancertrials.nci.nih.gov <p>Hormone receptor positive with symptomatic visceral disease:</p> <ul style="list-style-type: none"> Patients with extensive visceral or immediate life threatening disease might be optimally treated with initial chemotherapy and then considered for maintenance treatment with hormone therapy. Treatment choices include one of the following: <p>Combination Therapy</p> <ul style="list-style-type: none"> Anthracycline-based therapy (AC, FAC, CAF, FEC, CEF, EC) Doxorubicin – taxane (doxorubicin – paclitaxel or doxorubicin – docetaxel) Capecitabine – taxane (docetaxel or paclitaxel) CMF <p>Single Agent Therapy</p> <ul style="list-style-type: none"> Single-agent taxane therapy – Gemcitabine – Vinorelbine Single-agent anthracycline therapy – Infusional SFU – mas – paclitaxel (Abraxane) Capecitabine – Liposomal doxorubicin <ul style="list-style-type: none"> Clinical trials - Please refer to the following website for available clinical trials: http://cancertrials.nci.nih.gov <p>Hormone receptor negative, pre- and postmenopausal patients:</p> <ul style="list-style-type: none"> For patients who progress on chemotherapy, the treatment will depend on a number of factors, including previous therapy, patient symptoms, PS, and other patient specific considerations. Treatment can include combination or single-agent chemotherapy. <p>Combination Therapy</p> <ul style="list-style-type: none"> Anthracycline-based therapy (AC, FAC, CAF, FEC, CEF, EC) Doxorubicin – taxane (doxorubicin – paclitaxel or doxorubicin – docetaxel) Capecitabine – taxane (docetaxel or paclitaxel) CMF <p>Single Agent Therapy</p> <ul style="list-style-type: none"> Single-agent taxane therapy – Gemcitabine – Vinorelbine Single-agent anthracycline therapy – Infusional SFU – mas – paclitaxel (Abraxane) Capecitabine – Liposomal doxorubicin <ul style="list-style-type: none"> Clinical trials - Please refer to the following website for available clinical trials: http://cancertrials.nci.nih.gov <p>Her-2/neu overexpression (3+ Immunoperoxidase staining and/or 2+, 3+ by FISH) Patients</p> <ul style="list-style-type: none"> For patients with Her-2/neu protein overexpression (3+ immunoperoxidase staining and/or FISH+) who have progressed following first-line trastuzumab – chemotherapy, it is controversial whether trastuzumab plus another chemotherapy agent should be used as opposed to using chemotherapy alone. Trastuzumab alone is FDA approved as second line after progression on chemotherapy (without trastuzumab). However, in today's clinical practice, most patients receive trastuzumab initially: <ul style="list-style-type: none"> Trastuzumab alone Trastuzumab – Paclitaxel Trastuzumab – Paclitaxel – Carboplatin Trastuzumab – Docetaxel Trastuzumab – Docetaxel – Carboplatin Trastuzumab – Vinorelbine Trastuzumab – Capecitabine Clinical trials - Please refer to the following website for available clinical trials: http://cancertrials.nci.nih.gov 	<p>Stage IV</p> <ul style="list-style-type: none"> History and physical exam tailored to disease progression and therapy chosen. Routine use of X-rays, scans and serum markers in patients without symptoms is not recommended. Patients receiving tamoxifen should have a yearly gynecologic exam (if no prior hysterectomy) and should be carefully questioned regarding vaginal discharge or bleeding Patients receiving an aromatase inhibitor should have periodic monitoring of bone mineral density. Anti-resorptive therapy (preferable a non-SERM) should be considered if bone mineral density is depressed and all patients should take calcium and vitamin D The use of serum markers for following response in patients with recurrent disease should be restricted to patients in whom other objective measures are equivocal. Patients receiving bevacizumab – paclitaxel should be routinely monitored for hypertension, proteinuria, and bleeding. Cardiovascular events should be carefully monitored for but the benefits of the regimen clearly outweigh the risks. Patients receiving trastuzumab should have cardiac monitoring at 3, 6, and 12 months after beginning trastuzumab therapy. Trastuzumab therapy should be withheld for the following: <ul style="list-style-type: none"> If ejection fraction drops more than 10% below the institutional normal If the EF drops more than 15% overall Clinical CHF with a documented drop in EF If EF normalizes within 4 weeks may consider resuming trastuzumab therapy
<p>General Considerations regarding therapy choices:</p> <ul style="list-style-type: none"> Many chemotherapy combinations have been tested and have shown improved response rates compared with single agents. However, these combinations are generally more toxic than single agent therapy and most have shown no improvement in survival. Combination therapy over single agents should be considered in patients with good PS and in those with aggressive disease and visceral threat. If the patient has received prior anthracycline therapy, further anthracycline therapy may be considered if cardiac ejection fraction is normal. Additional options to consider include the use of a less toxic anthracycline (eg, epirubicin), liposomal doxorubicin, or a cardioprotectant (dexrazoxane). Patients with bone disease (especially those with lytic changes on x-ray) should be considered for bisphosphonate therapy in addition to chemo- or hormonal therapy. EBRT should be reserved for painful metastases or for lesions in which pathologic fractures are imminent or have already occurred. In general, bisphosphonate therapy should continue regardless of changes in a patient's chemotherapy regimen. Special considerations - see last page of guideline for treatment of patients with solitary metastases, spinal cord compression and other specialty situations. 					

Endocrine Regimens

AROMATASE INHIBITORS

Aromatase

Anastrozole 1 mg PO QD
For adjuvant therapy, continue for 5 years.
For Stage IV disease, continue until disease progression
Lancet 2002; 359:2131-2139.
Cancer 2003; 98:1802-1810.

Letrozole

Letrozole 2.5 mg PO daily until disease progression
JCO 2003; 21:2101-2109.
The Oncologist 2004; 9:497-506.

Exemestane (Aromasin)

Exemestane 25 mg PO daily
IV Engl J Med, 2004; 350:1091-1092. (adjuvant)
J Clin Oncol, 2000; 18:1399-1411. (metastatic)

LHRH AGONISTS

Goserelin

Goserelin acetate 3.6 mg SQ day 1
Repeat every 28 days x 2 years
Euro J Cancer, 2003; 39: 1711-1717 (adjuvant therapy)

or
Goserelin acetate 10.8 mg SQ day 1

Repeat every 3 months
JCO 1993;11:1529. (metastatic)

Goserelin + Tamoxifen

Goserelin 3.6 mg subcutaneously every 28 days for 3 years
Tamoxifen 20 mg PO daily for 5 years
JCO 2002; 20:4621-4627.

Leuprolide (monthly)

Leuprolide 7.5 mg IM day 1
Repeat every 28 days

Leuprolide (Q3 mo)

Leuprolide 22.5 mg IM day 1
Repeat every 3 months
* Leuprolide not FDA approved for breast cancer

OTHER

Faslodex

Faslodex 250mg IM Q28 days
J Clin Oncol, 2004; 22:1605-1613.

Megestrol acetate

Megestrol acetate 40 mg PO QID
Semin Oncol 1986; 13: 9 – 14

Tamoxifen

Tamoxifen 20 mg PO QD
Begin 2 – 5 weeks post-operatively
For adjuvant therapy, continue for 5 years. For Stage IV disease, continue until disease progression
J Clin Oncol, 2003; 21:2276 – 2281.

Toremifene

Toremifene 60 mg PO daily
JCO 1995;13:2556-2566.

Note: Mitoxantrone may be substituted for doxorubicin in patients who are elderly, or have cardiovascular disease, or have received prior anthracycline therapy. A = Adjuvant M = Metastatic Neo = neoadjuvant

Chemotherapy Regimens

Neoadjuvant Regimens

Docetaxel – Capecitabine

Docetaxel 75 mg/m² IV over 1 hour day 1
Capecitabine 1,000 mg/m² PO BID days 1 – 14
Repeat every 21 days x 4 cycles
ESMO 2004; abstract 215

Doxorubicin – Paclitaxel

Doxorubicin 60 mg/m² IV bolus over 5 – 15 minutes day 1
Paclitaxel 200 mg/m² IV over 3 hours day 1
Repeat every 21 days x 4 cycles
JCO 2004; 22:4958-4965.

Adjuvant Regimens

AC (A, M, Neo)

Doxorubicin 60mg/m² IV day 1
Cyclophosphamide 600mg/m² IVB day 1
Repeat every 21 days x 4 cycles
JCO 1990; 8:1483 – 1496.

CAF (A, M, Neo)

Cyclophosphamide 500mg/ m² IV day 1
Doxorubicin 50mg/ m² IV day 1
SFU 500 mg/ m² IV day 1
Repeat every 21 days x 6 cycles
Breast Can Res & Treat, 1983;3:209 – 220. (metastatic)
Proc Am Soc Clin Oncol, 1998;17:1a. Abstract 2

EAC (A, M, Neo)

SFU 500mg/m² IVB days 1 & 8
Doxorubicin 50mg/m² IVB day 1
Cyclophosphamide: 500mg/m² IVB day 1
Repeat every 21 – 28 days x 6 cycles
Ann Int Med 1975; 91:847

CEF (A, M, Neo)

Cyclophosphamide 75 mg/m² PO days 1 – 14
Epirubicin 60 mg/m² IV days 1 and 8
SFU 500 mg/m² IV days 1 and 8
Repeat cycle every 28 days x 6 cycles
JCO 1998; 16: 2651-2658

FEC-100 (A, M, Neo)

SFU 500 mg/m² IV day 1
Epirubicin 100 mg/m² IV day 1
Cyclophosphamide 800 mg/m² IV day 1
Repeat cycle every 21 days x 6 cycles
JCO 2001; 19: 602-611. (adjuvant)
JCO 2004; 22:3070-3079

FEC-100 – Docetaxel (A)

FEC-100 doses as above
Docetaxel 100 mg/m² IV day 1
Repeat every 21 days x 3 cycles followed by
SABC Symposium 2004. Abstract 27.

EC (A, M)

Epirubicin 100mg/m² IV day 1
Cyclophosphamide 830mg/m² IV day 1
Repeat cycle every 21 days
JCO 2001; 19: 3103 – 3110 (adjuvant)

CMF (IV-CTX) (A, M, Neo)

Cyclophosphamide 600 mg/m² IV day 1
Methotrexate 40 mg/m² IV day 1
SFU 600 mg/m² IV day 1
Repeat cycle Q21 days
Am J Med. 1987; 83:455

CMF (IV-CTX-D1,8) (A, M, Neo)

Cyclophosphamide 600mg/m² IV days 1 & 8
Methotrexate 40mg/m² IVB on days 1 & 8
SFU 600mg/m² IVB days 1 and 8
Repeat cycle Q 28 days x 6 cycles
Br J Cancer, 1999; 81 (2):316-322 (metastatic ref)

CMF (Oral - CTX) (A, M, Neo)

Cyclophosphamide 100 mg/m² PO days 1 – 14
Methotrexate 40 mg/m² IV days 1, 8
SFU 600 mg/m² IV days 1, 8
Repeat cycle Q28 days x 6 cycles
JCO 1990; 8(9):1493

Adjuvant Regimens (con't)

AC -> Paclitaxel (A, Neo)

Doxorubicin 60mg/m² IVB day 1
Cyclophosphamide 600mg/m² IVB day 1
Repeat every 21 days x 4 cycles followed by
Paclitaxel 175 mg/m² IV day 1
Repeat every 21 days x 4 cycles
JCO 2003; 21:976-983.

AC -> Docetaxel (A, Neo)

Doxorubicin 60mg/m² IV day 1
Cyclophosphamide 600mg/m² IV day 1
Repeat every 21 days x 4 cycles then
Docetaxel 100mg/m² IV day 1
Repeat every 21 days x 4 cycles
JCO 2003;21:4165

TAC

Taxotere 75 mg/m² IV day 1
Doxorubicin 50 mg/m² IV day 1
Cyclophosphamide 500 mg/m² IV day 1
Repeat every 21 days x 6 cycles
Proc Am Soc Clin Oncol, 2002; 36a. Abstract 141.
SABCS 2003; abstract 43

Dose-Dense AC -> Paclitaxel

Doxorubicin 60mg/m² IV day 1
Cyclophosphamide 600mg/m² IV day 1
Repeat every 14 days x 4 cycles followed by
Paclitaxel 175 mg/m² IV day 1 administered every 14 days x 4 cycles
G-CSF 300 or 480 mcg days 3 – 10 of each cycle
JCO 2003; 21:1431 – 1439.

Epirubicin – Tamoxifen (adjuvant for elderly)

Epirubicin 30 mg IV days 1, 8, 15
Tamoxifen 30 mg PO daily for 3 years
Repeat epiubicin every 28 days for 6 cycles
JCO 2004; 22:4674-4682.

AC – Paclitaxel + Trastuzumab

Doxorubicin 60mg/m² IV day 1
Cyclophosphamide 600mg/m² IV day 1
Repeat every 21 days x 4 cycles followed by
Paclitaxel 80 mg/m² IV weekly x 12 weeks is preferred (or 175 mg/m² IV day 1 every 21 days x 4 cycles)
Trastuzumab 4mg/kg loading dose for the 1st week followed by 2 mg/kg weekly for 51 weeks (total trastuzumab = 1 year). Trastuzumab should be given concurrently with Paclitaxel
Late-breaking session ASCO 2005 presented on May 16th, 2005 (results of NSABP-31/NCCCTG-N-9831)

Capecitabine Dose Calculation According to Body Surface Area

Surface Area (m ²)	Total Daily* Dose (mg)	Dose level 2500 mg/m ² /day	
		150 mg	500 mg
≤ 1.24	3000	0	3
1.25 - 1.36	3300	1	3
1.37 - 1.51	3600	2	3
1.52 - 1.64	4000	0	4
1.65 - 1.76	4300	1	4
1.77 - 1.91	4600	2	4
1.92 - 2.04	5000	0	5
2.05 - 2.17	5300	1	5
≥ 2.18	5600	2	5

* Total Daily Dose divided by 2 to allow equal morning and evening dose

Metastatic Combination Regimens

Doxorubicin – Docetaxel

Doxorubicin 50 mg/m² IV over 15 minutes on day 1 followed by
Docetaxel 75 mg/m² IV over 1 hour on day 1
Repeat every 21 days
JCO 2003; 21:968-975.

Doxorubicin – Paclitaxel

Doxorubicin 60 mg/m² IV day 1
Paclitaxel 150 mg/m² IV day 1
Repeat cycle every 21 days
Note: CSF support administered
JCO 2003; 21:588-592.

Docetaxel – Capecitabine

Docetaxel 75 mg/m² IV over 1 hour day 1
Capecitabine 1,250 mg/m² PO BID days 1 – 14
Repeat every 21 days
J Clin Oncol, 2002; 20:2812-2823. (1st and 2nd line metastatic)

Paclitaxel – Capecitabine

Paclitaxel 175 mg/m² IV over 3 hours day 1
Capecitabine 825 mg/m² PO BID days 1 – 14
Repeat every 21 days
JCO 2004; 22:2321 – 2327.

Trastuzumab – Paclitaxel

Trastuzumab Loading dose: 4 mg/kg IV over 90 minutes x 1
Maintenance dose: 2 mg/kg IV weekly over 30 minutes (if initial loading dose well tolerated)
Paclitaxel 175 mg/m² IV over 3 hours
Repeat Q21 days x 6 cycles
ASCO Proceedings 1998; 17: abstract 377

Trastuzumab – Paclitaxel – Carboplatin

Carboplatin AUC 6 IV on day 1
Paclitaxel 175 mg/m² IV over 3 hours
Trastuzumab 4mg/kg loading dose followed by a weekly dose of 2 mg/kg
Repeat every 21 days x 6 cycles
SABCS 2002; abstract 35.

Trastuzumab – Docetaxel

Docetaxel 100 mg/m² IV day 1
Trastuzumab 4mg/kg loading dose followed by a weekly dose of 2 mg/kg
Repeat every 21 days x 6 cycles (Herceptin continued until disease progression)
SABCS 2003; abstract 217.
JCO 2004; 22:1071 – 1077 (docetaxel may also be administered as 35 mg/m² weekly x 6 weeks; cycles repeated every 8 weeks)

Trastuzumab – Docetaxel – Carboplatin

Carboplatin AUC 6 IV day 1
Docetaxel 75 mg/m² IV day 1
Trastuzumab 4mg/kg loading dose followed by weekly 2 mg/kg
Repeat every 21 days x 6 cycles (continue trastuzumab for 1 year or until disease progression)
JNCI 2004;96:759-769.

Trastuzumab – Vinorelbine

Trastuzumab 4mg/kg loading dose followed by weekly 2 mg/kg
Vinorelbine 25 mg/m² IV weekly over 10 min following trastuzumab
Repeat weekly until progression
JCO 2003; 21:2895-2895.

Trastuzumab – Capecitabine

Trastuzumab 4mg/kg loading dose followed by weekly 2 mg/kg
Capecitabine 1250 mg/m² PO BID days 1 – 14 (max of 6 cycles)
Repeat every 21 days (trastuzumab may be con't until disease prog.)
SABCS 2004; abstract 3049.

Trastuzumab – Gemcitabine

Trastuzumab 4mg/kg loading dose followed by weekly 2 mg/kg
Gemcitabine 1,200 mg/m² IV days 1 and 8
Repeat gemcitabine every 21 days
Clin Breast Cancer, 2004; 5:142-147.

Gemcitabine – Paclitaxel

Gemcitabine 1,200 – 1,250 mg/m² IV on days 1 and 8
Paclitaxel 175 mg/m² IV on day 1
Repeat every 21 days for 8 cycles
Oncology 2004; 66:18 – 23. (G = 1,200 mg/m²)
Proc Am Soc Clin Oncol, 2004; 22: Abstract 510 (G = 1,250 mg/m²)

Bevacizumab – Paclitaxel

Bevacizumab 10 mg/m² on days 1 and 15
Paclitaxel 90 mg/m² on days 1, 8, 15
Repeat every 28 days
Late-breaking ASCO 2005 abstract presented on May 16th, 2005

Carboplatin – Paclitaxel (weekly)

Carboplatin AUC 2 IV day 1
Paclitaxel 100 mg/m² IV day 1
Repeat cycles weekly
JCO 2002; 20:3857-3864.

Single-Agent Metastatic Regimens

Docetaxel

Docetaxel 60 – 100 mg/m² IV day 1
Repeat every 21 days
J Clin Oncol, 1999; 18:3362-3368.

Docetaxel (Weekly)

Docetaxel 35 – 40 mg/m² IV day 1 weekly x 6 weeks
Repeat every 8 weeks
JCO 2000;18:1212-19 (40 mg/m²)
JCO 2001;19:3500-3505 (36 mg/m²)

Doxorubicin

Doxorubicin 60 mg/m² IV day 1
Repeat cycle Q21 – 28 days
Drugs. 1992;44(Suppl 4):17.
Am JCO. 1989;12:57 – 62.
JCO 2003; 21:588-592

Doxorubicin (weekly)

Doxorubicin 20 mg/m² IV weekly
Eur J Cancer, 1994;30A:1775.

SFU

SFU 300 mg/m²/day CIV
Continue until progression or unacceptable toxicity.
JCO. 1995;13: 4119 – 423.

Epirubicin

Epirubicin 70 mg/m² IV days 1 and 8
Repeat every 28 days
Cancer Chemother Pharmacol 2000;46:459-466
OR
Epirubicin 90 mg/m² IV day 1
Repeat every 21 days
Br J Cancer 1998;77:2257-2263.

Trastuzumab

Trastuzumab Loading dose 4 mg/kg IV over 90 minutes x 1;
Maintenance dose 2 mg/kg IV weekly over 30 minutes
(if initial loading dose well tolerated)
ASCO Proceedings 1998;17:abstract 376.

Capecitabine

Capecitabine 2510 mg/m² PO QD (divided dose given twice daily) days 1 – 14
Repeat Q21 days
JCO 1999; 17: 465-493.

Capecitabine (elderly)

Capecitabine 1,000 mg/m² PO daily (divided dose given BID) days 1 – 14
Repeat cycle every 21 days
JCO 2005 (early release)

Paclitaxel

Paclitaxel 175 mg/m² IV day 1 over 3 hours or over 24 hours
Repeat every 21 days
JCO 1995; 13:2575
JCO 2003; 21:588-592

Paclitaxel (Weekly)

Paclitaxel 60 – 90 mg/m² IV day 1
Repeat weekly
JCO 1998;16:3353-3361 (reference uses 100 mg/m² weekly)

Vinorelbine

Vinorelbine 30 mg/ m² IV day 1
Repeat every 7 days
JCO 1995;13:2567.

Gemcitabine

Gemcitabine 1200 mg/m² days 1,8,15
Repeat Q28 days
Breast Cancer Res Treat 2001;66: 83 – 87
Oncology 2002;62:2-8

Liposomal doxorubicin

Liposomal doxorubicin 50 mg/m² IV day 1
Repeat every 21 – 28 days
J Clin Oncol 2004; 22:3893 – 3901.

Liposomal Ara-C (intrathecal)

50 mg IT Q2 weeks x 1 month.

Intrathecal Methotrexate

12mg IT 1-2 times per week initially followed by therapy every 1-2 weeks after symptom improvement

nab – paclitaxel (Abraxane)

nab – paclitaxel 260 mg/m² IV over 30 minutes day 1

Repeat every 3 weeks

SABCS 2003; abstract 44

nab – paclitaxel (Abraxane – weekly)

nab – paclitaxel 125 mg/m² IV over 30 minutes day 1 weekly x 3

Repeat every 4 weeks

ASCO 2004 (O'Shaughnessy J et al)

Radiation

Stage 0 - DCIS

4500-5040 cGy is delivered to the entire breast in daily fractions of 180-200 cGy. Radiation is delivered through tangential opposed fields.

A boost of 1000-1500 to the primary site may be considered

Stage I

A dose of 4500-5040 cGy to the entire breast delivered at 180-200 cGy/day 5 days/week. A boost of 1000-2000 cGy is usually delivered to the tumor bed.

Palliative Regimens - Examples of possible radiation regimens follow - there are other acceptable regimens

Spinal Cord Compression

Acceptable regimens include the following:

- 400 cGy x 3, then 200 cGy x 12
- 300 cGy x 10 to total 3000 cGy
- 250 cGy x 15 to total 3750 cGy
- 200 cGy x 20 to total 4000 cGy

Bone Metastases

Acceptable regimens include the following:

- 800-1000 cGy in 1 fraction
- 400 cGy x 5
- 300 cGy x 10
- 250 cGy x 15-16

Stage II

A dose of 4500-5040 cGy to the entire breast & nodes delivered at 180-200 cGy/day 5 days/week. A boost of 1000-2000 cGy is usually delivered to the tumor bed.

Palliative Regimens - Examples of possible radiation regimens follow - there are other acceptable regimens

Spinal Cord Compression

Acceptable regimens include the following:

- 400 cGy x 3, then 200 cGy x 12
- 300 cGy x 10 to total 3000 cGy
- 250 cGy x 15 to total 3750 cGy
- 200 cGy x 20 to total 4000 cGy

Bone Metastases

Acceptable regimens include the following:

- 800-1000 cGy in 1 fraction
- 400 cGy x 5
- 300 cGy x 10
- 250 cGy x 15-16

Stage IIIA

A dose of 4500-5040 cGy to the entire breast and nodal regions delivered at 180-200 cGy/day 5 days/week. A boost of 1000-2000 cGy is usually delivered to the tumor bed.

Palliative Regimens - Examples of possible radiation regimens follow - there are other acceptable regimens

Spinal Cord Compression

Acceptable regimens include the following:

- 400 cGy x 3, then 200 cGy x 12
- 300 cGy x 10 to total 3000 cGy
- 250 cGy x 15 to total 3750 cGy
- 200 cGy x 20 to total 4000 cGy

Bone Metastases

Acceptable regimens include the following:

- 800-1000 cGy in 1 fraction
- 400 cGy x 5
- 300 cGy x 10
- 250 cGy x 15-16

Stage IIIB

A dose of 4500-5040 cGy to the entire breast and nodal regions delivered at 180-200 cGy/day 5 days/week. A boost of 1000-2000 cGy is usually delivered to the tumor bed.

Palliative Regimens - Examples of possible radiation regimens follow - there are other acceptable regimens

Spinal Cord Compression

Acceptable regimens include the following:

- 400 cGy x 3, then 200 cGy x 12
- 300 cGy x 10 to total 3000 cGy
- 250 cGy x 15 to total 3750 cGy
- 200 cGy x 20 to total 4000 cGy

Bone Metastases

Acceptable regimens include the following:

- 800-1000 cGy in 1 fraction
- 400 cGy x 5
- 300 cGy x 10
- 250 cGy x 15-16

Stage IV

A dose of 4500-5040 cGy to the entire breast and nodal regions delivered at 180-200 cGy/day 5 days/week. A boost of 1000-2000 cGy is usually delivered to the tumor bed.

Palliative Regimens - Examples of possible radiation regimens follow - there are other acceptable regimens

Spinal Cord Compression

Acceptable regimens include the following:

- 400 cGy x 3, then 200 cGy x 12
- 300 cGy x 10 to total 3000 cGy
- 250 cGy x 15 to total 3750 cGy
- 200 cGy x 20 to total 4000 cGy

Bone Metastases

Acceptable regimens include the following:

- 800-1000 cGy in 1 fraction
- 400 cGy x 5
- 300 cGy x 10
- 250 cGy x 15-16

Patient Education

LCIS

- Perform monthly breast exam
- Recommend screening and counseling of relatives if a positive family history is identified (males, if carriers also need counseling)
- Tamoxifen information
- Lifestyle modifications
 - weight loss
 - decrease alcohol consumption
 - low fat diet
 - increase exercise
- Educate women about symptoms of recurrence

DCIS

- Perform monthly breast exam
- Recommend screening and counseling of female relatives if a positive family history is identified
- Tamoxifen information
- Lifestyle modifications
 - weight loss
 - decrease alcohol consumption
 - low fat diet
 - increase exercise
- Educate women about symptoms of recurrence

Stages I-IV

- Recommend joining a self help or support group (for Stage I-IV patients)
- Perform monthly breast exam
- Recommend screening and counseling of female relatives if a positive family history is identified
- Educate women about symptoms of recurrence
- Inform care provider about use of alternative medicines such as herbs (some can lead to interactions with other drugs)
- Lifestyle modifications
 - weight loss
 - decrease alcohol consumption
 - low fat diet
 - increase exercise
- Patients on statin therapy for lipid management should also be made aware that it may also be associated with a decrease in the risks of breast and colon cancers.

Drug Complications

SFU:

Most Common: Myelosuppression: granulocytopenia nadir: 7-14 days; thrombocytopenia nadir: 7-14 days
Gastrointestinal: nausea and vomiting, stomatitis, diarrhea, proctitis, esophagitis
Less Common: Alopecia; hyperpigmentation of nail bed, face and hands; partial loss of nails; maculopapular rash
Rarely: Acute cerebellar syndrome

Cyclophosphamide:

Most Common: Leukopenia, nadir occurs @ 7-14 days, recovery after 10 days, mild anemia, thrombocytopenia, hemorrhagic cystitis: 5-10% of patients, alopecia, anorexia, nausea, vomiting
Less Common: Amenorrhea, urticaria, transverse rigging of nails, skin hyperpigmentation, SLE/DH, hepatotoxicity
Rarely: Anaphylaxis, cardiotoxicity, pulmonary toxicity, increased incidence of transitional cell CA of the bladder.

Methotrexate:

Most Common: Nausea, vomiting, anorexia, stomatitis, diarrhea, myelosuppression with pancytopenia: RBC nadir 6-13 days; neutrophils, 2-7 days; WBC's nadir: 4-7 days (rarely again at 12-21 days); pleuritis nadir: 5-12 days
Less Common: Hepatic fibrosis, cirrhosis (usually high dose MTX); renal tubular necrosis (high dose regimens); alopecia, dermatitis, pigment changes, dizziness, malaise, blurred vision
Rarely: Chills, fever, osteopenia, conjunctivitis, anaphylaxis.

Tamoxifen:

Most Common: Mild and transient leukopenia and thrombocytopenia can occur in 5-10% of patients. Menopause-like symptoms: hot flashes, nausea, vomiting occur in < 25% of patients.
Less Common: vaginal bleeding, vaginal discharge, menstrual irregularities, pruritis vulvae, skin rashes, dizziness, headache, depression, lassitude, leg cramps, slight peripheral edema
Rare: Retinitis, pseudotumor cerebrae, deep-vein thrombosis

Doxorubicin:

Most Common: Myelosuppression: mild to moderate, nausea, vomiting, diarrhea, alopecia
Less Common: Radiation call reaction, radiosensitization, skin hyperpigmentation, dermal cresses, fever, chills, allergic reaction, conjunctivitis.
Cumulative Dose Toxicity: Cardiac - CHF cardiomyopathy

Letrozole

Maculoleukelated pain, nausea, vomiting, headache, fatigue, diarrhea, constipation, hot flashes, peripheral edema.

Docetaxel

Leukopenia, nadir occurs @ 7-8 days, anemia, thrombocytopenia, fluid retention (peripheral edema), hypersensitivity reactions (including flushing rash, dyspnea, hypertension), asthenia, nausea, vomiting, stomatitis, alopecia, transient skin changes, arthralgia and/or myalgia

Goserelin

Hot Flashes, Nausea/Vomiting, Impotence, Loss of libido

Prednisone

GI upset, peptic ulceration, higher susceptibility to infection, decreased glucose intolerance, electrolyte disturbance, paper-thin skin with striae, behavioral abnormalities, acne.

Dosing for Bisphosphonates

Pamidronate 90mg IV every 21-28 days
Zoledronic acid 4mg IV every 21-28 days

Tocopherol

Hot flashes, sweating, nausea, vaginal discharge, dizziness, edema, cataracts, vomiting, thrombophlebitis.

Mifostiprone

Most Common: cough or SOB, GI bleeding, leukopenia, stomach pain, stomatitis or mucositis.
Less Frequent or Rare: arrhythmias, CHF, conjunctivitis, jaundice, renal failure, seizures, thrombocytopenia, allergic reaction, extravasation, local irritation, or phlebitis.

Anastrozole

Flushing, nausea, increased bone and/or tumor pain, breast pain, confusion, thrombophlebitis

Exemestane (Aromasin)

Hot flashes, nausea, fatigue, increased sweating, increased appetite, androgenic symptoms, peripheral edema

Megestrol Acetate

Most Common: breakthrough bleeding and anemorrhoea, abdominal pain or cramping, edema, headache, mood changes, weight gain.
Less Frequent or rare: rash, depression, thromboembolism, breast pain or tenderness, hot flashes, insomnia, nausea.

Capecitabine

Nausea, vomiting, diarrhea, stomatitis, hand and foot syndrome, fatigue, paresthesias, anorexia, lymphopenia, neutropenia, thrombocytopenia, hyperbilirubinemia

Trastuzumab (Herceptin)

Parathesia, fever, chills, headache, CHF (more likely in combination therapy), nausea, vomiting, diarrhea, rash, peripheral edema

Erlotinib (Tarceva)

Major Dose Limiting: Leukopenia, neutropenia
Hematologic: Leukopenia, neutropenia, anemia, febrile neutropenia
GI Effects: Nausea, mucositis, diarrhea, anorexia, abdominal pain
Other: Alopecia, hot flashes, leukemia

Liposomal Ara-C (Intralipid) (DepoCyt)

Headache, arachnoiditis

Vinorelbine

Major Dose Limiting: Granulocytopenia, leukopenia
Hematologic: as above and anemia (mild)
GI Effects: nausea, vomiting, constipation, diarrhea, rise in total bilirubin, rise in SGOT
Nervous System Effects: peripheral neuropathy, asthenia
Other: injection site reactions, pain, phlebitis, alopecia, dyspnea

Paclitaxel

Most Common: hypersensitivity Rxns (less common with pre-medication), neutropenia, leukopenia, anemia, peripheral neuropathies, alkaline phosphatase elevation, alopecia, myalgia/arthralgia, radiation recall

Leuprolin

Hot Flashes, Nausea/Vomiting, Impotence, Loss of libido

Breast Cancer - AJCC Staging Handbook - 6th Edition

Primary Tumor (T):

- T1: Tumor 2.0 cm or less in greatest dimension
T1c: Micrometastasis 0.1 cm or less in greatest dimension
T1a: 0.5 cm or less
T1b: More than 0.5 cm but not more than 1 cm in greatest dimension
T1c: More than 1 cm but not more than 2 cm in greatest dimension
T2: Tumor more than 2 cm but not more than 5 cm in greatest dimension
T3: Tumor more than 5 cm in greatest dimension
T4: Tumor of any size with direct extension to chest wall or skin
T4a: Extension to chest wall, not including pectoralis muscle
T4b: Edema, ulceration of the skin of the breast, or satellite skin nodules confined to the same breast
T4c: Both T4a and T4b
T4d: Inflammatory carcinoma

Regional lymph nodes (N)

N0: No regional lymph node metastasis or only clumps of cells by immuno-histochemistry but not by H&E staining (N0+)

- N1: No regional lymph node mets histologically, negative IHC
N10 (+): No regional lymph node mets histologically, positive IHC, no IHC cluster > 0.2 mm
N10 (mol -): negative molecular findings
N10 (mol +): positive molecular findings

N1: Metastasis to movable ipsilateral axillary lymph node(s)

- pN1: metastases in 1-3 axillary lymph nodes and/or in internal mammary nodes with microscopic disease detected by SLND but not clinically
pN1a: 1-3 axillary nodes
pN1b: Mets in internal mammary nodes with microscopic disease detected by SLND but not clinically apparent
pN1c: metastases in 1-3 axillary lymph nodes and in internal mammary nodes with microscopic disease detected by SLND but not clinically

N2: Metastasis to ipsilateral lymph node(s) fixed or matted or in clinically apparent ipsilateral internal mammary nodes in the absence of clinically evident axillary lymph node metastases

- pN2: Metastases in 4-9 axillary lymph nodes or in clinically apparent ipsilateral internal mammary nodes in the absence of clinically evident axillary lymph node metastases
pN2a: metastases in 4-9 nodes with at least one tumor deposit > 2.0 mm
pN2b: Mets in clinically apparent internal mammary nodes in the absence of axillary lymph node metastases

N2c: Metastases in ipsilateral axillary lymph node(s) fixed or matted to one another or to other structures

N2c: Metastases only in clinically apparent ipsilateral internal mammary nodes and in the absence of clinically evident axillary lymph node metastases

N3: Metastases in ipsilateral infraclavicular lymph nodes with or without axillary lymph node involvement or in clinically apparent ipsilateral nodes and in the presence of clinically evident axillary lymph node metastases; or metastases in ipsilateral supra-clavicular lymph nodes with or without axillary or internal mammary lymph node involvement

- pN3: metastases in 10 or more axillary lymph nodes, infraclavicular lymph nodes or in clinically apparent ipsilateral internal mammary lymph nodes in the presence of 1 or more positive nodes or in > 3 nodes with clinically negative micro-sopic metastasis in internal mammary nodes; or in ipsilateral supra-clavicular nodes.
N3a/pN3a: Metastases in 10 or more axillary nodes or metastases to the ipsilateral infraclavicular lymph nodes
N3b/pN3b: Metastases in ipsilateral internal mammary lymph nodes and axillary lymph nodes
N3c/pN3c: Metastases in ipsilateral supra-clavicular lymph nodes

Distant Metastases (M)

- M0: No distant metastases
M1: Distant metastasis present

Pegfilgrastim *(PEG-fill-GRASS-tim)*

Brand Name: Neulasta® *(Noo-lasta)*

Patient Education Quick Reference Guide

Uses For This Medication

- Many chemotherapy medications reduce the number of germ fighting white blood cells, which increases the risk of infection. Pegfilgrastim helps to prevent this by increasing the number of white blood cells in patients who are receiving chemotherapy.
- This medication may also be given for other conditions as determined by your doctor.

How This Medication Works

Pegfilgrastim is known as a "colony stimulating factor" or "white blood cell growth factor". This medication is a man-made version of a substance that is naturally produced in your body which helps the bone marrow to make new white blood cells. Your doctor or healthcare provider may recommend that you have regular blood tests to count the number of white blood cells in your body. It is important that you follow your doctor or healthcare provider's instructions about these tests.

Benefits Of This Medication

Pegfilgrastim is given to prevent your white blood cell levels from becoming too low during chemotherapy treatment. This helps prevent the development of infections and helps to ensure that you will continue to receive your chemotherapy medications on time at the appropriate dose.

Who Should Not Take This Medication

You should not take this medication if you:

- Are allergic to other products made using a bacteria called *E coli*
- Are allergic to filgrastim, pegfilgrastim or any of its components

Precautions To Be Aware Of Before Taking This Medication

Allergy related precautions

The parent drug of pegfilgrastim is called filgrastim. Rarely, filgrastim may cause allergic reactions. These allergic reactions can cause rash, hives, shortness of breath, wheezing, a drop in blood pressure, swelling around the mouth or eyes, fast pulse, or sweating. Although allergic reactions have not been reported with pegfilgrastim, it is possible for them to occur. Your doctor or healthcare provider will watch you carefully during and after the administration of pegfilgrastim to make sure that you do not experience any allergic reactions. If you are receiving pegfilgrastim at home, you should tell your doctor or healthcare provider about any allergic type symptoms. If an allergic reaction occurs it is treatable with medications.

Precautions (continued)

Blood related precautions

- The parent drug of pegfilgrastim is called filgrastim. Filgrastim has been reported to cause severe sickle cell crisis in patients who have sickle cell disease. If you have sickle cell disease, make sure that you tell your doctor or healthcare provider.
- Although pegfilgrastim can reduce the risk of infection, it may not prevent all infections. An infection can still happen when your white blood cell levels are low. You should watch for symptoms of an infection such as fever (temperature of 100.5 °F or higher), chills, sore throat, diarrhea, or redness, swelling, or pain around a cut. If you think you might have an infection, let your doctor or healthcare provider know immediately.

Organ related precautions

- The parent drug of pegfilgrastim is called filgrastim. Filgrastim has been reported to cause acute respiratory distress syndrome (ARDS). This is a life-threatening condition in which swelling and fluid build up in the lungs and leads to low oxygen levels in the blood. If you develop difficulty breathing, you should let your doctor or healthcare provider know immediately.
- The parent drug of pegfilgrastim is called filgrastim. Rarely, filgrastim has been reported to cause problems with your spleen (splenic rupture). Symptoms can include pain in the upper left portion of the abdomen or in the shoulder. Although a rupture of the spleen has not been reported with pegfilgrastim, it is possible for it to occur. Report any abdominal pain to your doctor or healthcare provider immediately.

Patient specific precautions

- It is not known if this medication is safe and effective in children.

Pregnancy and breastfeeding precautions

- When taking this medication, you should use effective birth control to prevent pregnancy. Tell your doctor or healthcare provider right away if you or your spouse/partner becomes pregnant since this medication may cause fetal harm.
- It is not known whether this medication is found or excreted in breast milk. Since many medications are excreted in breast milk and because this medication can cause serious harmful reactions in infants, breastfeeding should be avoided.

Administration related precautions

Pegfilgrastim should not be given during the time between 14 days before and 24 hours after chemotherapy, or while you are receiving radiation therapy.

Medication And Food Interactions

Before using this medication, tell your doctor or healthcare provider of all prescription or over-the-counter products you are taking, including dietary supplements or vitamins, herbal medicines and homeopathic remedies. Do not start or stop any medication without your doctor or healthcare provider's approval. Possible interactions can occur with pegfilgrastim and the following medications:

- Lithium

Side Effects

- All medications can cause side effects. However, not all patients will experience these side effects. In addition, other side effects not listed can also occur in some patients. You should call your doctor or healthcare provider if you have any questions or concerns while you are on this medication.
- You should contact your doctor or healthcare provider if you experience any side effect(s) which do not go away, worsen, are serious in nature, or are worrisome to you.

Side Effects (continued)

More common side effects

- Bone and/or muscle pain [Acetaminophen (Tylenol) may be taken for pain relief (follow package directions)]
- Redness, swelling, or itching at site of injection

Rare side effects

- Allergic reaction which can cause rash, itching, red blotches, swollen face or lips, difficulty breathing (see Precautions To Be Aware Of Before Taking This Medication)
- Enlarged or ruptured spleen (see Precautions To Be Aware Of Before Taking This Medication)

How To Take This Medication

- This medication is usually given by an injection under the skin (subcutaneous or SC injection) but can also be given by injection into a vein (IV).
- If you or a family member are giving or receiving the pegfilgrastim injection at home, you should review the detailed information provided by the drug manufacturer on this subject. Read this information carefully and make sure that you understand how to prepare the injection, how to properly use the disposable syringes, and how to give the injection. If you have any questions about this information, check with your doctor or healthcare provider.
- When this medication is given as an injection under the skin (subcutaneous), there are four common areas where injections may be given:
 - The outer area of your upper arms
 - The abdomen, except for the two inch area around your navel
 - The front of your middle thighs
 - The upper outer areas of your buttocks

It is best to rotate the areas where the injection is given to avoid soreness. It is best to avoid giving an injection in areas that are tender, red, bruised, hard, or that contain scars or stretch marks.

- In the unlikely event of an overdose of this medication contact your doctor, your local poison control center at 1-800-222-1222, or emergency services immediately.

Proper Storage

- Unopened containers should be stored in the refrigerator. Keep in original package to protect from light.
- Before being injected, pegfilgrastim may be allowed to reach room temperature for a maximum of 48 hours. During this time it should still remain in the original package protected from light.
- Keep the used syringes and needles in a special container.
- Keep this medication out of the reach of children or pets.
- Ask your doctor or healthcare provider how to dispose of any medication that you no longer use.

Disclaimer

This handout is to provide you with additional information about pegfilgrastim. It is not a substitute or replacement for the expertise and judgment of your healthcare provider. The information is not intended to cover all possible uses, directions, precautions, medication interactions, or side effects. In addition, this information should not be interpreted to suggest that the use of a particular medication is safe, appropriate, or effective for you. You should always talk with your healthcare provider before starting or stopping any medication.

Additional Instructions for Patient:

AGENDA ITEM 2

Memorandum

To: Licensing Committee

Date: March 9, 2006

From: Patricia Harris 
Executive Officer

Subject: Proposed Regulation to Recognize Approved
Accreditation Entities and Evaluation Factors

Background on B & P § 4127.1

B & P § 4127.1 requires pharmacies compounding sterile injectable drug products to obtain a license from the board. In order to obtain such a license the pharmacy must first be inspected by the board and found in compliance with board standards for sterile compounding. The law exempts pharmacies that are accredited by the Joint Commission on the Accreditation of Healthcare Organizations or other accrediting agencies approved by the board from the license requirement as specified in Section 4127.1 (d). Exempted pharmacies must still comply with board regulations regarding sterile injectable compounding, but do not have to obtain a separate license.

The Board approved Accreditation Commission for Health Care (ACHC) as an accrediting entity in April 2003. The board granted this approval for 3 years. At that time, ACHC accredited both home infusion pharmacies and specialty pharmacies that deliver biotech drugs and other specialty products.

In July 2003, the board also approved Community Health Care Accreditation Program (CHAP) as an accreditation agency. CHAPS is a national non-profit accreditation organization established in 1965 to accredit community-based health care organizations.

Information on ACHC and CHAP and its accreditation processes will be provided at the meeting.

In 2003, the Licensing Committee developed the following criteria for the evaluation of applications by accrediting entities for board approval. The following criteria are the result of the Licensing Committee's discussions, including a presentation to the Committee by an ACHC surveyor.

The factors are:

1. **Periodic inspection** – The accrediting entity must subject the pharmacy to site inspection and re-accreditation at least every three years.

2. **Documented accreditation standards** – The standards for granting accreditation and scoring guidelines for those standards must reflect both applicable California law and sound professional practice as established by nationally recognized professional or standard setting organizations.
3. **Evaluation of surveyor’s qualifications** – The surveyors employed to perform site inspections must have demonstrated qualifications to evaluate the professional practices subject to accreditation.
4. **Acceptance by major California payors** – Recognition of the accrediting agency by major California payors (e.g., HMOs, PPOs, PBGH, CalPERS).
5. **Unannounced inspection of California accredited sites** – The board must conduct unannounced inspections of two or more accredited sites and find those sites in satisfactory compliance with California law and good professional practice.
6. **Board access to accreditor’s report on individual pharmacies.**
7. **Length of time the accrediting agency has been operating.**
8. **Ability to accredit out-of-state pharmacies.** Non-resident pharmacies are eligible for licensure under the sterile compounding statutes and accreditation should be equally available to both resident and non-resident pharmacies.

AGENDA ITEM 3

Memorandum

To: Licensing Committee

Date: March 9, 2006

From: Patricia Harris 
Executive Officer

Subject: Approval of Accrediting Entities

Background on B & P § 4127.1

B & P § 4127.1 requires pharmacies compounding sterile injectable drug products to obtain a license from the board. In order to obtain such a license the pharmacy must first be inspected by the board and found in compliance with board standards for sterile compounding. The law exempts pharmacies that are accredited by the Joint Commission on the Accreditation of Healthcare Organizations or other accrediting agencies approved by the board from the license requirement as specified in Section 4127.1 (d). Exempted pharmacies must still comply with board regulations regarding sterile injectable compounding, but do not have to obtain a separate license.

The Board approved Accreditation Commission for Health Care (ACHC) as an accrediting entity in April 2003. The board granted this approval for 3 years. In July 2003, the board also approved Community Health Care Accreditation Program (CHAP) as an accreditation agency.

Since both agencies have requested that the Board of Pharmacy approve them again as accreditation agencies, and if the approval is granted, it is being recommended that the board pursue a regulation to recognize these agencies in regulation as the Joint Commission on the Accreditation of Healthcare Organizations is recognized in statute.

In addition, it is suggested to include the factors that are considered for approval as an accreditation agency to be included in the regulation, including a method by which the board may no longer recognize an agency. If the board agrees with this recommendation, proposed language will be drafted.

The factors are:

Factors to Consider

The evaluation of accrediting agencies for board approval under Business and Professions Code section 4127.1 should be based on the accrediting agency's ability to evaluate the pharmacy's conformance with California law and good professional practice standards. The following factors should be considered when making such an evaluation:

1. **Periodic inspection** – The accrediting entity must subject the pharmacy to site inspection and re-accreditation at least every three years.
2. **Documented accreditation standards** – The standards for granting accreditation and scoring guidelines for those standards must reflect both applicable California law and sound professional practice as established by nationally recognized professional or standard setting organizations.
3. **Evaluation of surveyor's qualifications** – The surveyors employed to perform site inspections must have demonstrated qualifications to evaluate the professional practices subject to accreditation.
4. **Acceptance by major California payors** – Recognition of the accrediting agency by major California payors (e.g., HMOs, PPOs, PBGH, CalPERS).
5. **Unannounced inspection of California accredited sites** – The board must conduct unannounced inspections of two or more accredited sites and find those sites in satisfactory compliance with California law and good professional practice.
6. **Board access to accreditor's report on individual pharmacies.**
7. **Length of time the accrediting agency has been operating.**
8. **Ability to accredit out-of-state pharmacies.** Non-resident pharmacies are eligible for licensure under the sterile compounding statutes and accreditation should be equally available to both resident and non-resident pharmacies.

AGENDA ITEM 4

Memorandum

To: Licensing Committee

Date: March 9, 2006

From: Patricia Harris 
Executive Officer

Subject: Request to Extend the Waiver for the Study
"Evaluation of the Impact of Pharmacists in the
Prevention of Medication Errors"

In April 2004, the Board of Pharmacy granted a waiver for the study by UCSF School of Pharmacy and Cedars-Sinai Medical Center entitled, "Evaluation of the Impact of Pharmacists in the Prevention of Medication Errors Associated with Prescribing and Administration in the Hospital Setting." The wavier was granted for two years.

This study was a sequel to the successful experimental program that evaluated pharmacy technicians checking another pharmacy technician in a unit-dose drug distribution system in a hospital pharmacy.

This purpose of the sequel study is to evaluate the impact of pharmacists in prevention of medication errors associated with prescribing and administering of medications as a result of pharmacists being re-deployed from unit-dose medication cassette checking to more clinical and professional functions. Such functions require special expertise of pharmacists in the management of drug therapy, from which patients will benefit.

Preliminary data from the study was provided to the board at its July meeting. At its last meeting, the board approved a regulation change to allow a specialized trained pharmacy technician to check another pharmacy technician in a unit-dose drug distribution system in a hospital pharmacy that has a clinical program. The proposed regulation change is scheduled for the April board meeting. If the board approves the proposed regulation, it will take approximately 6-9 months before the regulation would become effective.



March 8, 2006

Patricia F. Harris
Executive Director
California State Board of Pharmacy
1625 North Market Blvd, Suite N219
Sacramento, CA 95834

Dear Ms. Harris,

We would like to request the opportunity to discuss an extension of the waiver for the study by the UCSF School of Pharmacy and Cedars-Sinai Medical Center entitled, "Evaluation of the Impact of Pharmacists in the Prevention of Medication Errors Associated with Prescribing and Administration in the Hospital Setting," at the March 22, 2006 Licensing Committee Meeting. The two-year study was approved by the State Board of Pharmacy on April 21, 2004. After the Board of Pharmacy's approval, the study was subsequently reviewed and approved by the Institutional Review Board at Cedars-Sinai Medical Center and the Committee on Human Research at UCSF. Therefore, in order to complete the data collection, analysis and review of the results, we would like to request an extension until December 31, 2006. Please free to contact me should you have any questions. Thank you for your consideration.

Sincerely,

A handwritten signature in black ink, appearing to read 'Peter J. Ambrose'.

Peter J. Ambrose, Pharm.D., FASHP
Professor of Clinical Pharmacy
UCSF School of Pharmacy
C-152, Box 0622
San Francisco, CA 94143-0622
Long Beach Office: 562-933-0289

A handwritten signature in black ink, appearing to read 'Rita Shane'.

Rita Shane, Pharm.D., FASHP
Director, Pharmacy Services
Cedars-Sinai Medical Center
Assistant Dean, Clinical Pharmacy
UCSF School of Pharmacy
Los Angeles, CA
310-423-5611
shane@cshs.org

cc: Frank Saya, Pharm.D.

**Board of Pharmacy
Specific Language**

Amend Section 1793.7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1793.7 Requirements for Pharmacies Employing Pharmacy Technicians.

- (a) Except as otherwise provided in section 1793.8, any Any function performed by a pharmacy technician in connection with the dispensing of a prescription, including repackaging from bulk and storage of pharmaceuticals, must be verified and documented in writing by a pharmacist. Except for the preparation of prescriptions for an inpatient of a hospital and for an inmate of a correctional facility, the pharmacist shall indicate verification of the prescription by initialing the prescription label before the medication is provided to the patient.
- (b) Pharmacy technicians must work under the direct supervision of a pharmacist and in such a relationship that the supervising pharmacist is fully aware of all activities involved in the preparation and dispensing of medications, including the maintenance of appropriate records.
- (c) A pharmacy technician must wear identification clearly identifying him or her as a pharmacy technician.
- (d) Any pharmacy employing or using a pharmacy technician shall develop a job description and written policies and procedures adequate to ensure compliance with the provisions of Article 11 of this Chapter, and shall maintain, for at least three years from the time of making, records adequate to establish compliance with these sections and written policies and procedures.
- (e) A pharmacist shall be responsible for all activities of pharmacy technicians to ensure that all such activities are performed completely, safely and without risk of harm to patients.
- (f) For the preparation of a prescription for an inpatient of a licensed health facility and for a patient of a licensed home health agency, the ratio shall not be less than one pharmacist on duty for a total of two pharmacy technicians on duty. Pursuant to Business and Professions Code section 4115(g)(1), this ratio shall not apply to the preparation of a prescription for an inmate of a correctional facility of the Department of the Youth Authority or the Department of Corrections, or for a person receiving treatment in a facility operated by the State Department of Mental Health, the State Department of Developmental Services, or the Department of Veterans Affairs.

Note: Authority cited: Sections 4005, 4007, 4038, 4115 and 4202, Business and Professions Code.

Reference: Sections 4005, 4007, 4038, 4115 and 4202, Business and Professions Code.

Adopt Section 1793.8 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1793.8 Technicians in Hospitals with Clinical Pharmacy Programs.

(a) A general acute care hospital, as defined in Health and Safety Code 1250 (a), that has an ongoing clinical pharmacy program may allow pharmacy technicians to check the work of other pharmacy technicians in connection with the filling of floor and ward stock and unit dose distribution systems for patients admitted to the hospital whose orders have previously been reviewed and approved by a licensed pharmacist.

Only inpatient hospital pharmacies as defined in 4029(a) that maintain a clinical pharmacy services program as described in 4052 may have a technician checking technician program as described. The pharmacy shall have on file a description of the clinical pharmacy program prior to initiating a technician checking technician program.

(1) This section shall only apply to acute care inpatient hospital pharmacy settings.

(2) Hospital pharmacies that have a technician checking technician program shall deploy pharmacists to the inpatient care setting to provide clinical services.

(b) Compounded or repackaged products must have been previously checked by a pharmacist and then may be used by the technician to fill unit dose distribution systems, and floor and ward stock.

(c) To ensure quality patient care and reduce medication errors, programs that use pharmacy technicians to check the work of other pharmacy technicians pursuant to this section must include the following components:

(1) The overall operation of the program shall be the responsibility of the pharmacist-in-charge.

(2) The program shall be under the direct supervision of a pharmacist and the parameters for the direct supervision shall be specified in the facility's policies and procedures.

(3) The pharmacy technician who performs the checking function has received specialized and advanced training as prescribed in the policies and procedures of the facility.

(4) To ensure quality there shall be ongoing evaluation of programs that use pharmacy technicians to check the work of other pharmacy technicians.

Note: Authority cited: Sections 4005, 4007, 4038, 4115, and 4202, Business and Professions Code.

Reference cited: Sections 4007, 4038, 4115 and 4202, Business and Professions Code.



University of California
San Francisco

June 16, 2005

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2005 JUN 20 AM 11:04

LA/OC Area Clerkship Program
Department of
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Long Beach, CA 90801-1428
tel: 562/933-0289
fax: 562/933-2348

Patricia F. Harris
Executive Director
California State Board of Pharmacy
400 "R" Street, Suite 4070
Sacramento, CA 95814-6200

Re: Technician Study – Interim Report

Dear Ms. Harris:

As per the waiver approved by the Board of Pharmacy, I am submitting an interim report of the study conducted at Cedars-Sinai Medical Center: **Evaluation of the Impact of Pharmacists in the Prevention of Medication Errors Associated with Prescribing and Administration of Medications in the Hospital Setting.** The attached document summarizes the results for the first 48 weeks of the study.

The results to date demonstrate that having specially-trained pharmacy technicians perform the non-discretionary task of checking technician-filled unit-dose medication carts frees up pharmacist time and enables pharmacists to play a critical role in intercepting potential medication errors and preventing harm to patients.

The study is continuing and the results will be presented to the Board upon completion. Should you need additional information about the progress of the experimental program, do not hesitate to contact me at (562) 933-0289.

Respectfully submitted,

Peter J. Ambrose, Pharm.D.
Professor of Clinical Pharmacy
School of Pharmacy
University of California, San Francisco

Enclosure

Cc: Frank Saya, Pharm.D.
Rita Shane, Pharm.D.

**Evaluation of the Impact of Pharmacists in the
Prevention of Medication Errors Associated
with Prescribing and Administration of
Medications in the Hospital Setting
Summary of Results
June 21st 2004 - May 22nd 2005**



A Collaborative Study Between
UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
SCHOOL OF PHARMACY
and the
Pharmacy Services Department of
CEDARS-SINAI MEDICAL CENTER

Background

- Study to determine the impact of pharmacists on prevention of medication errors during the equivalent time spent on checking medication cassettes
- 2 year study (waiver) allows technicians to check technicians filled medication cassettes
- The number and types of medication errors prevented at the prescribing step (order written by the physician) and at the administration step (medication administered by the nurse) of the medication use process will be reported

Study Objectives

- Determine top 10 drugs involved in potential prescribing and administration errors
- Determine type and frequency of medication errors intercepted at the prescribing and administration steps
- Compare intercepted errors with USP MedMARX data on errors
- Evaluate factors contributing to prescribing and medication administration errors
- Evaluate potential harm that could have resulted if error was not intercepted

Medication Related Encounters

June 21st 2004 - May 22nd 2005 (48 weeks)

Total Medication Related Encounters: **28,969 (603/week)**

- Potential Errors Intercepted (prevented): **1296**
 - Medication Prescribing : 885 (68%)
 - Medication Administration: 411 (32%)
- Other Medication Related Encounters :
 - Pharmacist dosing per MD request: 25,342
 - STAT orders: 360
 - Rounds: 58
 - Code Blue: 29
 - Drug Information: 1661

Medication Prescribing Potential Errors Intercepted

June 21st 2004 - May 22nd 2005 (48 weeks)

- Potential prescribing errors prevented by the pharmacist: 885
- Orders requiring clarification: 534 (type of error not specified)
- Types of medication ***errors intercepted which prevented****:

Wrong Dose	48.9 %	Medication Contraindicated	3.1 %
Allergy Contraindication	21.7 %	Drug Interaction	2.3 %
Necessary medications not ordered	11.7 %	Wrong Frequency/Rate	2.0 %
Duplication in therapy	5.7 %	Wrong Drug	0.6 %
Wrong Route	4.0 %		

* In those situations where error type was specified

Additionally, there were 57 incomplete orders requiring clarification.

Examples of Medication Prescribing Errors Prevented

<u>Problem Identified</u>	<u>Pharmacist Recommendation</u>	<u>Outcome Avoided</u>
Ganciclovir: 5mg/kg iv q12h pt s/p kidney transplant & renal insufficiency	Pharmacist recommended 2.5mg/kg/day for CMV induction	Avoided adverse drug reaction (ADR) from overdose
Oxaliplatin (chemotherapy) dosage in patient with renal insufficiency	Pharmacist recommended dosage adjustment	Avoided ADR due to excessive dose of chemotherapy
Celebrex ordered in patient with sulfa allergy	Pharmacist recommended alternative	Avoided morbidity associated with an allergic reaction
Ceftazidime ordered as 1 gm q8h for meningitis in young patient	Pharmacist recommended 2 gm q8h to achieve adequate effect	Avoided sub-optimal treatment, possible mortality/morbidity
Lovenox 40 mg daily ordered in patient with chronic renal failure	Pharmacist recommended change to Heparin	Avoided increased risk of bleeding in patient already receiving blood transfusions

Medication Administration

Potential Errors Intercepted

June 21st 2004 - May 22nd 2005 (48 weeks)

Potential medication administration errors prevented by a pharmacist: 411 encounters

Types of medication ***errors intercepted which prevented:***

Omission of Dose	41.2 %	Wrong Rate	5.5 %
Transcription Error	13.9 %	Wrong Drug	4.8 %
Wrong Dose	8.1 %	Drug to be given to	
Wrong Patient	6.0 %	patient was not ordered	3.8 %
Extra Dose	7.9 %	Wrong Route	3.1 %
Delay in Dose	5.7 %		

Examples of Medication Administration Errors Prevented

<u>Problem Identified</u>	<u>Pharmacist Recommendation</u>	<u>Outcome Avoided</u>
Pt. scheduled for chemotherapy in AM.	Pharmacist identified that chemo was not given	<i>Avoided omission of chemotherapy</i>
Pt was about to receive Tobramycin at a 12 hr interval; order was for q24h	Pharmacist notified nurse that dose was to be given every 24 hr	<i>Avoided potential renal (kidney) toxicity</i>
PCA pump was programmed incorrectly	Pharmacist notified nurse	<i>Avoided potential adverse events associated with excessive narcotic dose</i>
Pt receiving Potassium Chloride 60meq infusion; order was for 20meq	Pharmacist notified nurse to change infusion	<i>Avoided potential hyperkalemia and cardiac arrest</i>
Nurse transcribed Kayexalate when Kaopectate ordered	Pharmacist notified nurse about transcription error	<i>Avoided potential hypokalemia and cardiac toxicity</i>

Results compared to USP MedMARX Data

Leading types of errors include:

	USP MedMarx Data 2003 ¹	Research Study
Omission error	24 %	22.7 %
Improper dose/quantity	23 %	26.4 %
Unauthorized drug	10 %	2.1 %
Extra dose	5 %	4.2 %
Wrong patient	5 %	3.3 %
Wrong route	2 %	3.4 %

1. http://www.magnetmail.net/actions/email_web_version.ofm?recipient_id=9223078&message_id=63691&user_id=USP

TOP 10 Medications/Classes

June 21st 2004 - May 22nd 2005 (48 weeks)

Top 10 medications/classes involved in potential prescribing and administration errors

Medication Prescribing

- Chemotherapy
- Electrolytes
- Enoxaparin (Lovenox)
- Vancomycin
- Warfarin
- Levofloxacin
- Neupogen
- Fluconazole
- Cefepime
- TPN

Medication Administration

- Vancomycin
- Heparin
- Chemotherapy
- Electrolytes
- TPN
- Erythropoietin
- Warfarin
- Fluconazole
- Insulin
- Levofloxacin

Preliminary Evaluation of Potential Patient Outcomes

Pharmacist prevented medications errors associated with potential harm: 422

No Harm	340
Temporary Harm	387
Permanent Harm	11
Increase in Length of Stay	23
Death	1
Type of harm unspecified	534

Factors Contributing to Prescribing Errors

- Incomplete patient information
- Drug allergies overlooked
- Wrong drug name, dosage form or abbreviation
- Incorrect dosage calculations
- Incorrect dosage frequency
- Laboratory results not checked prior to ordering medications
- Concomitant therapy (e.g. supportive drugs for chemotherapy) necessary to prevent adverse reactions not ordered

Factors Contributing to Administration Errors

- Two patient identifiers not used
- Illegible orders
- Drug name confusion
- Incorrect pump programming
- Patients transferred and orders not transcribed accurately
- Environmental factors- distractions, interruptions and significant workload
- Staffing issues- such as shift changes and floating staff

Summary of Study Results to Date

Results of the 48 week study demonstrates the impact of pharmacists on prescribing and administration errors:

- 1296 errors intercepted by the pharmacist
- 27450 medication related encounters including dosing of medications per MD request, participation in codes, rounds and drug information questions
- Preliminary evaluation of outcomes: 422 pharmacist encounters prevented potential harm of which:
 - 387 prevented temporary harm
 - 11 prevented permanent harm
 - 23 prevented an increase in length of stay
 - 1 prevented death

AGENDA ITEM 5

Memorandum

To: Licensing Committee

Date: March 9, 2006

From: Patricia Harris 
Executive Officer

Subject: NABP Partnership with Educational Credential
Evaluators, Inc. (ECE)

Attached is information from the National Association of Boards of Pharmacy (NABP) regarding its partnership with ECE for the educational credential evaluation of applicants to the Foreign Pharmacy Graduate Examination Committee (FPGEC) Certification Program. This partnership will change the method by which foreign pharmacy graduates will be evaluated.

ECE will be responsible for verifying the educational background of the applicant and NABP will verify the applicant's professional licensing and registration information. The foreign graduate will submit all documents directly to ECE for evaluation.

This new partnership is intended to address the increase of workload that this program has experienced over the last few years and improve the processing time for these applicants.

California requires all foreign graduates to be FPGEC certified before they can apply to be licensed as an intern or pharmacist.

EXECUTIVE OFFICERS – STATE BOARDS OF PHARMACY

February 24, 2006

Page 2

then sends the ECE application form to ECE along with official transcripts, official proof of degree, and \$85. The applicant also sends the FPGEC Application Form for Examination and Certification Program to NABP along with required documentation and \$700.

While ECE verifies the educational background information, NABP verifies the applicant's professional licensing and registration information. Following NABP's receipt of a General Evaluation Report from ECE verifying the applicant's educational equivalency and completion of the Association's own licensure and registration verification processes, the qualifying applicant receives an FPGEE acceptance letter. An applicant's receipt of the FPGEE acceptance letter allows him or her to sit for the Foreign Pharmacy Graduate Equivalency Examination (FPGEE). After receiving a passing grade on the FPGEE, along with passage of the Test of English as a Foreign Language (TOEFL), Test of Spoken English (TSE), or TOEFL Internet-based Test (iBT), applicants obtain the FPGEC Certificate. The FPGEC Certificate allows foreign-educated and licensed pharmacists to move forward towards licensure in the US.

If you have any questions, please contact me via phone at 847/391-4400 or 1-800/774-6227 or via e-mail at mdickson@nabp.net. Thank you.

cc: NABP Executive Committee
NABP Advisory Committee on Examinations
Carmen A. Catizone, Executive Director/Secretary



News Release

FOR IMMEDIATE RELEASE

March 9, 2006

**For more information contact:
Larissa Doucette, Editorial Manager
847/391-4405; custserv@nabp.net**

NABP Partners with ECE for FPGEC Educational Credential Evaluations

The National Association of Boards of Pharmacy[®] (NABP[®]) is pleased to announce that it has formed a partnership with the Educational Credential Evaluators, Inc (ECE) to evaluate the educational credentials of applicants to the Foreign Pharmacy Graduate Examination Committee[™] (FPGEC[®]) Certification Program. Beginning April 14, 2006, FPGEC applicants will be required to submit their supporting educational credential documents to ECE.

The improved processing time that the new method is designed to achieve has resulted in the first increase of the \$700 FPGEC fee in 21 years. Applicants will pay an additional \$85 fee for ECE to evaluate an applicant's educational credentials.

Founded in 1980, ECE is a not-for-profit public service organization specializing in the evaluation of foreign educational credentials. ECE has identified the United States equivalence of foreign educational credentials for more than 1,000 educational institutions, employers, and professional licensing boards for over 20 years.

The FPGEC Certification program is accepted by the majority of NABP's member boards of pharmacy as a means of documenting the educational equivalency of an applicant's foreign pharmacy education as well as the pharmacist's licensure and/or registration. Foreign-educated

(— more —)

pharmacists awarded FPGEC Certification are considered to have partially fulfilled eligibility requirements for licensure in those states that accept the Certification.

For more information, please contact NABP at 847/391-4406 or via e-mail at custserv@nabp.net. Information and registration forms as well as further details of program requirements may be found on NABP's Web site at www.nabp.net.

NABP is the independent, international, and impartial Association that assists its member boards and jurisdictions in developing, implementing, and enforcing uniform standards for the purpose of protecting the public health.

AGENDA ITEM 6

Memorandum

To: Licensing Committee

Date: March 9, 2006

From: Patricia Harris 
Executive Officer

Subject: Accreditation Council for Pharmacy Education
(ACPE)

Attached is an announcement from ACPE regarding the change in its accreditation procedures. After June 30, 2006, ACPE will require that any new doctor of pharmacy program seeking preaccreditation status must progress through both stages of preaccreditation, which is precandidate and candidate phases, before consideration of full accreditation. Prior to this policy change, it was not essential that a program be granted precandidate status before students were admitted.

After June 23, 2006, a new program must achieve precandidate status before admitting students. Should a new program admit students without achieving precandidate status, this will preclude ACPE from considering the program's application for candidate preaccreditation status, and full accreditation cannot be considered until graduation of the first class. Students graduating from a program without candidate status will thus have graduated from a program with no accreditation status and will likely not be eligible for licensure.

This change in policy is consistent with the board's recent regulation change that states that the board will recognize a school of pharmacy that is accredited or granted candidate status by ACPE or schools recognized by the board. The board has recently "recognized" new schools of pharmacy that have been granted precandidate status so that the students can be registered as interns.

Report on ACPE Site Visits

Board members have been actively participating on the ACPE evaluation teams for the California schools of pharmacy. President Goldenberg participated in the recent evaluation of Western University of Health Sciences College of Pharmacy. Former board member Darlene Fujimoto was on the team that evaluated UC San Diego Skaggs School of Pharmacy. The evaluation conflicted with the board's February meeting so Dr. Fujimoto graciously agreed to be the board's representative. Board member Ruth Conroy will be on the site team for Loma Linda University School of Pharmacy scheduled for April 18th – 20th. ACPE is scheduled to evaluate the Touro University California College of Pharmacy for candidate status on April 25-27, 2006, which conflicts with the board's April meeting. I am waiting to hear if they will reschedule the date. Otherwise I will again be seeking a former board member as our representative on the site team.



To: <stbdpharm@listserv.acpe-accredit.org>
CC:
Subject: ACPE Accreditation Procedure Change

stbdpharm-request@list
serv.acpe-accredit.org

02/24/2006 12:20 PM

February 24, 2006

Dear ACPE Stakeholder:

The Accreditation Council for Pharmacy Education (ACPE) announces a change in its accreditation procedures. After June 30, 2006, ACPE requires that any new doctor of pharmacy program seeking preaccreditation status progress through both stages of preaccreditation, precandidate and candidate phases, before consideration of full accreditation. Prior to this policy change, it was not essential, although highly recommended, that a program be granted precandidate status before students were admitted. After June 30, 2006, a new program must achieve precandidate status. Should a new program admit students without achieving precandidate status, this will preclude ACPE from considering the program's application for candidate preaccreditation status, and full accreditation cannot be considered until graduation of the first class. Students graduating from a program without candidate status will thus have therefore graduated from program with no accreditation status and will likely not be eligible for licensure.

The full text of Section 9.3 as revised of the Policies and Procedures section of the ACPE Accreditation Manual is attached below.

9.3 Preaccreditation. A newly instituted Doctor of Pharmacy program of a College or School of Pharmacy must be granted each of the two preaccreditation statuses at the appropriate stage of its development. The standards are the same as those employed for accredited status, however, preaccreditation involves, in large measure, planning in accord with standards and provision of reasonable assurances for a quality outcome. It should be noted that a new program must achieve precandidate accreditation status prior to the enrollment of students.

Failure to do so will preclude consideration for ACPE accreditation until after

graduates have been produced, at which time a program could be considered for full accreditation status. As these first graduates would emerge from a program with no accreditation status, they may not be eligible for licensure as pharmacists.

9.3.1 Precandidate. A new program that has no students enrolled but that meets the eligibility criteria for accreditation may be granted Precandidate accreditation status. The granting of Precandidate status indicates that a College or School's planning for the Doctor of Pharmacy program has taken into account ACPE standards and guidelines and suggests reasonable assurances of moving to the next step, that of Candidate status. Granting of Precandidate status brings no rights or privileges of accreditation. Full public disclosure by the College or School of Pharmacy of the terms and conditions of this accreditation status is required.

9.3.2 Candidate. Once students have enrolled in a new program, but the program has not had a graduating class, the program may be granted Candidate status. The granting of Candidate status denotes a developmental program, which is expected to mature in accord with stated plans and within a defined time period. Reasonable assurances are expected to be provided that the program may become accredited as programmatic experiences are gained, generally, by the time the first class has graduated. Graduates of a class designated as having Candidate status have the same rights and privileges as graduates of an accredited program.

Upon granting preaccreditation status (Precandidate or Candidate) to a program, or in the event of voluntary withdrawal from preaccreditation, or upon a decision to let preaccreditation lapse, written notification of such action shall be made to the U.S. Secretary of Education, the appropriate state licensing or authorizing agency, the appropriate regional and/or other accrediting agencies, and the public within 30 days. Public notification includes presentation on the ACPE web site.

Sincerely,

Jeffrey W. Wadelin, Ph.D.

Associate Executive Director and

Director, Professional Degree Program Accreditation



ACCREDITATION COUNCIL FOR PHARMACY EDUCATION

20 North Clark Street, Suite 2500 • Chicago, Illinois 60602-5109 • www.acpe-accredit.org
312/664-3575 • FAX 312/664-4652 • E-mail: jwadelin@acpe-accredit.org

Jeffrey W. Wadelin, Ph.D.
Associate Executive Director and
Director, Professional Degree Program Accreditation

February 28, 2006

Darlene Fujimoto, PharmD
Associate Director
Medical Affairs
Biogen Idec
5200 Research Place
San Diego, CA 92122

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Dear Darlene,

We certainly appreciated the opportunity to work with you during the on-site visit to the University of California, San Diego, Skaggs School of Pharmacy & Pharmaceutical Sciences on January 31 – February 2, 2006. Your participation added to the success of the visit.

I look forward to seeing you soon at NABP and other professional gatherings.

Thanks again for all your help.

Sincerely,

cc: Patricia Harris, Executive Officer, California State Board of Pharmacy

AGENDA ITEM 7



California State Board of Pharmacy
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www.pharmacy.ca.gov

STATE AND CONSUMERS AFFAIRS AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
ARNOLD SCHWARZENEGGER, GOVERNOR

To: Board Members

Date: March 13, 2006

From: Board of Pharmacy

Subject: Competency Committee Report

New Content Outline and Handbook for CPJE

At the October 2005 board meeting, the board approved the use of the new content outline for the California Pharmacist Jurisprudence Examination (CPJE) given on or after April 1, 2006. The board posted the updated Content Outline on the Web site. The content outline that will be used until April 1, 2006, is posted on the Web site as well.

The California Pharmacy Jurisprudence Examination Handbook is currently being updated to include the new Content Outline as well as a sample CPJE exam. The anticipated effective date of the new handbook is April 1, 2006. The sample CPJE exam will be posted separately on the Web site prior to April 1, 2006.

Test Administration Contract

The Office of Examination Resources (OER) within the Department of Consumer Affairs is renewing its contract with a vendor to provide computer based testing. OER conducted the bidders' sessions on March 3 & 6, 2006. Final bids are due to OER on March 28, 2006. The cost opening is scheduled for April 7, 2006, with a Notice of Intent to Award the Contract on April 12, 2006. The anticipated contract award date is April 28, 2006. The duration of the contract is 3 years with 2 one-year optional extensions.

CPJE Statistics

The next CPJE statistical report will cover performance data for 10/1/05-3/31/06. This report should be available at the April board meeting.