OVERVIEW OF NUCLEAR PHARMACY & TERMINOLOGY

OBJECTIVES:

Upon completion of this session the student will be able to:

1. Describe the design of a hospital nuclear pharmacy.
2. Describe the daily operation of a nuclear pharmacy
3. Explain the difference between a pharmaceutical and a radiopharmaceutical
4. List the characteristics of the ideal diagnostic radiopharmaceutical
5. List the characteristics of a therapeutic radiopharmaceutical

Design and Daily Operations of a Nuclear Pharmacy

In order for a nuclear medicine procedure to be performed, some type of radiopharmaceutical must be given to the patient.

Prior to administration the radiopharmaceutical must be prepared, pass quality assurance test and be assayed to determine the administered dose in a nuclear pharmacy or "hot" lab.

The design should consider:

- The best use of space
- Logical and functional work spaces
- The radiation safety of personnel working in the area.

A nuclear pharmacy must be an area:

1. Which can be secured
2. With adequate shielding to keep area and personnel radiation exposure levels "As Low As Reasonably Achievable" (should be below 2 mR/hr, usually less than 0.5 mR/hr)
3. Which is clean and free from contamination
4. Which allows for the disposal of radioactive waste and nonradioactive waste in separate containers and also considers biohazardous waste
5. Which is in close proximity to the imaging area if in-house or to the clinical facility if it is a commercial pharmacy

Nuclear Pharmacy features:

The work areas surfaces should be stainless steel or laminated, covered with imperviously backed absorbent paper

Fumehood, if volatile substances, xenon gas or radioiodines, are being stored or used

Leaded drawing stations and lead bricks

Syringe and vial shields

Lab monitors and survey meters

DAILY OPERATION

The day begins with the elution of Mo-99/Tc-99m generator to obtain ^{99m}Tc04, sodium pertechnetate.

[All other radiopharmaceutical which are labeled with other radionuclides, ^{111}In, ^{67}Ga, etc. are supplied by a commercial radiopharmacy]

The pertechnetate must be checked for molybdenum content.

Assayed activities of ^{99m}Tc04 are then added to vials containing certain pharmaceuticals, "kits"

The radiopharmaceutical preparations are then checked for radiochemical purity.

Single patient doses are then drawn up to meet the prescribed doses

Personnel who compounds "kits" or dispenses radiopharmaceutical doses should wear a lab coat, whole body badge, usually a film or Luxel badge, and extremity badge, usually a TLD ring badge, and gloves.

Tongs should be used to handle unshielded vials which are being assayed.

RADIOPHARMACEUTICALS V.S. PHARMACEUTICALS

Radioactive	Not Radioactive
Do Not Modify Function	Modify Function
(No Drug Effect)	(Has Drug Effect)
Minimal Chemical or Elemental weight	Higher chemical Composition
Concentration changes with time	Concentration stable

25 mg of Lasix is the same today, tomorrow and next week.

25 mCi of ^{99m}Tc-DTPA is only 25 mCi at the time that activity is determined.

RADIONUCLIDE + PHARMACEUTICAL = RADIOPHARMACEUTICAL

^{99m}Tc04 + DTPA = ^{99m}Tc-DTPA

DIAGNOSTIC V.S. THERAPEUTIC RADIOPHARMACEUTICALS

Diagnostic radiopharmaceuticals are used to determine a disease or disorder.

Therapeutic radiopharmaceuticals are used to treat a previously diagnosed disease or disorder.

Diagnostic radiopharmaceuticals should have the following characteristics:

1 - Should have a short effective half-life

$$Te = \frac{Tp \times Tb}{Tp + Tb}$$

The rule of thumb is that the effective half-life (Te) cannot be longer than the shorter of the physical (Tp) or biological (Tb) half-life.

2 - Should decay by a process which yields gamma rays only

Electron capture and isomeric transition

Gamma rays of 150 keV are the best

3 - Should have no particulate emissions

No alpha or beta particles

Not Detectable by cameras & High radiation dose to patient

4 - Should be easy to obtain for clinical use

(diagnostic Rp, cont)

5 - Should give a high target-to-nontarget activity ratio

The target is activity in the organ to be imaged.

The nontarget is activity in surrounding tissues and organs.

High ratio = clear image of target organ

Low ratio = blurred image - poor contrast

A therapeutic radiopharmaceutical should have different characteristics:

1 - Should have particulate emissions, which gives a higher radiation dose to the target organ

2 - Should have a relatively long effective half-life (days)

3 - Should have a moderately high activity level which is intended to kill cells

Given to treat a disease or disorder, such as polycythemia, thyroid cancer or hyperthyroidism and chronic bone pain.

PRODUCTION OF RADIOPHARMACEUTICALS

OBJECTIVES:

Upon completion of this session the student will be able to:

1. List the three methods of production of radio-pharmaceuticals used in nuclear medicine
2. Explain the operation of a reactor.
3. List the radionuclides produced by a reactor
4. Explain the operation of a cyclotron.
5. List the radionuclides produced by a cyclotron
6. Explain the operation of a $^{99}Mo/^{99m}Tc$ generator.

There are three principle methods of production of radionuclides used in nuclear medicine:

REACTORS, CYCLOTRONS and GENERATORS

A **REACTOR** is a device which uses the fission of uranium to create energy, or in our case useable radionuclides.

Uranium-235 is a fissionable by slow neutron bombardment.

The **by-products** of fission are two smaller atoms & 2-3 fast neutrons

If the by-product neutrons are slowed down the will cause fission of other ^{235}U atoms, liberating other neutrons = self-sustaining reaction

Uranium-239 decays to Plutonium-239 which is also fissionable. Pu-239 in the fuel rod increases the neutron flux.

Fuel rods - U-235

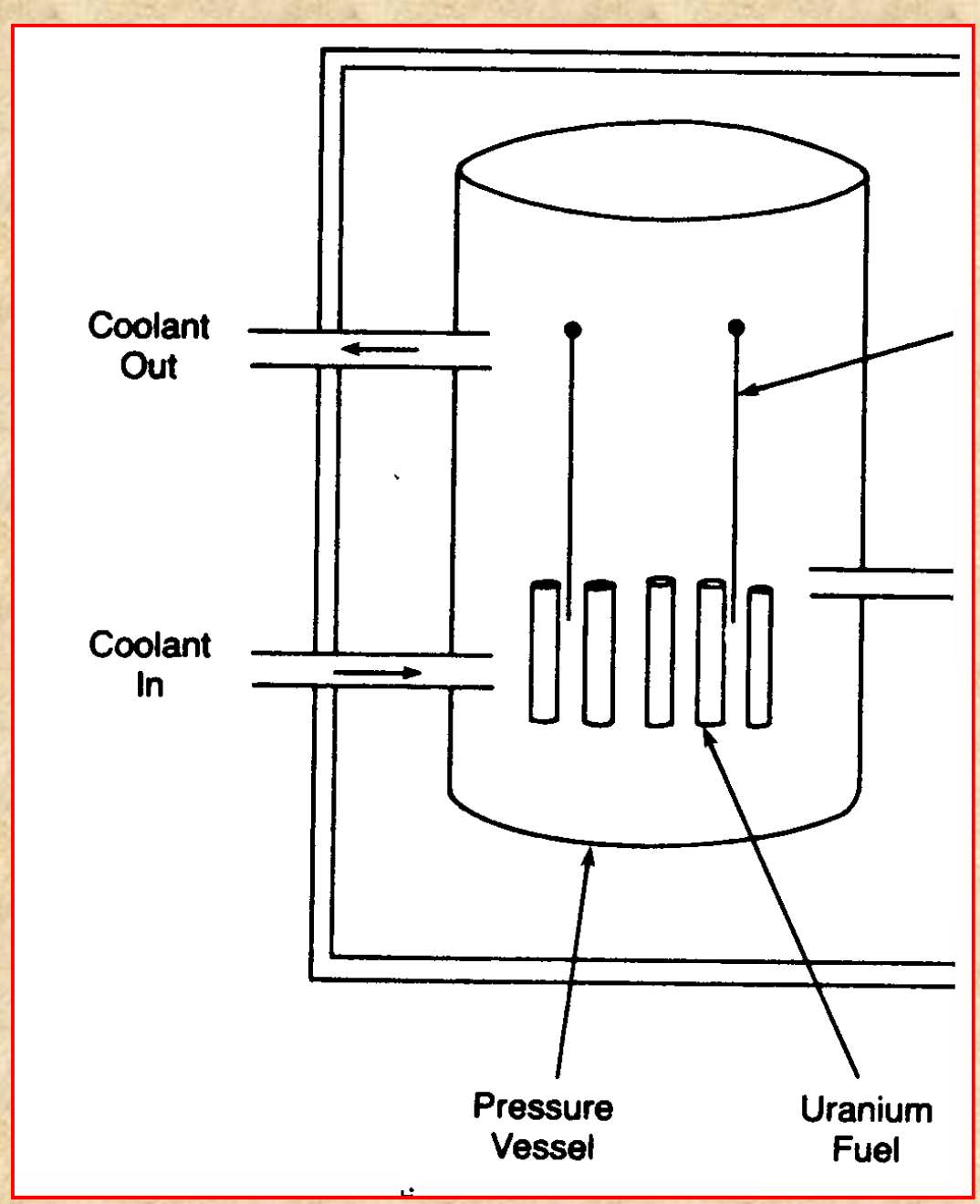
Moderators - Graphite(slow down fast neutrons)
- Water (cool down reaction)

Control Rods -Boron & Cadmium
(absorb neutrons to control reaction)

"Spent" uranium contains by-product radionuclides:

I-131	I-125	H-3
Cs-137	Co-60	P-32
Mo-99	Sr-89	
Xe-133		

Nuclear Reactor



A CYCLOTRON is a accelerator which propels charged particles in a circular path

PARTS:

Two hollow, metal Dees
A large electromagnet
A voltage supply

- Charged particles move from side-to-side because of the alternating charge on the DEES

- The magnetic poles bend the path into a circle

- Charged particles can be a proton(s) or combination of proton & neutron

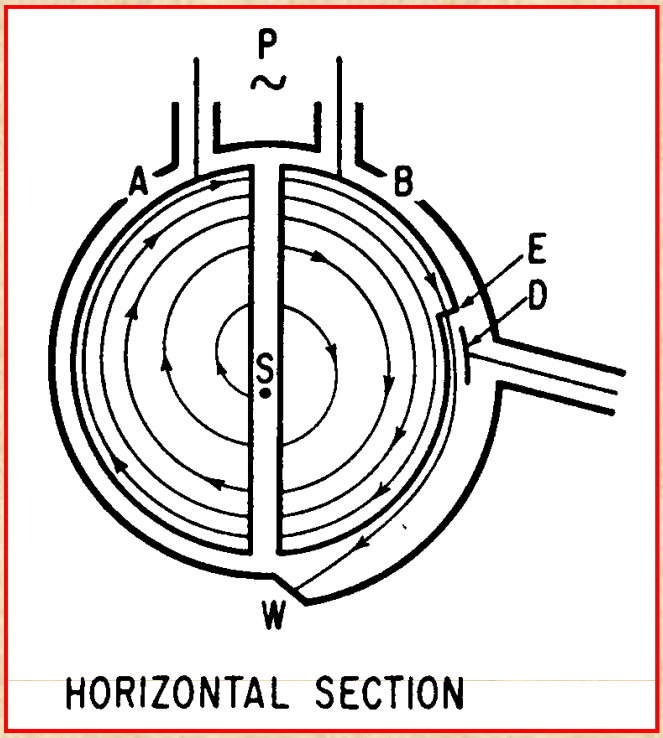
- Radionuclides produced by cyclotron

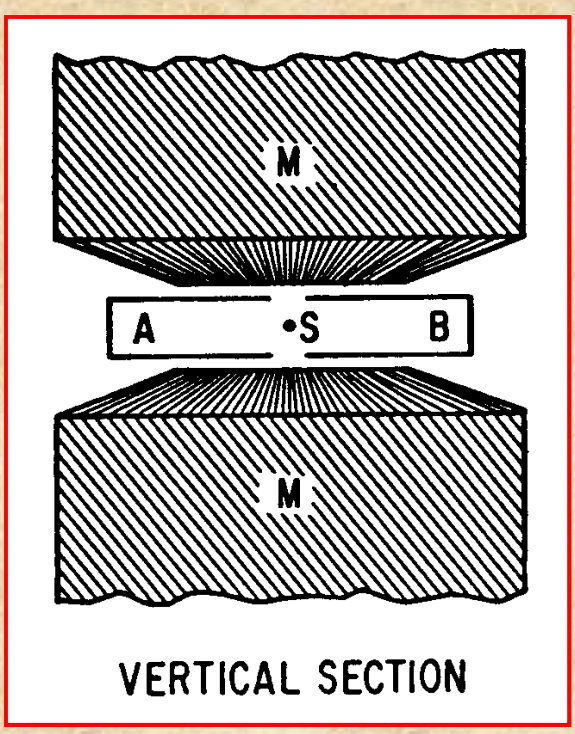
Tl-201, Ga-67, I-123, In-111

Short lived radionuclides

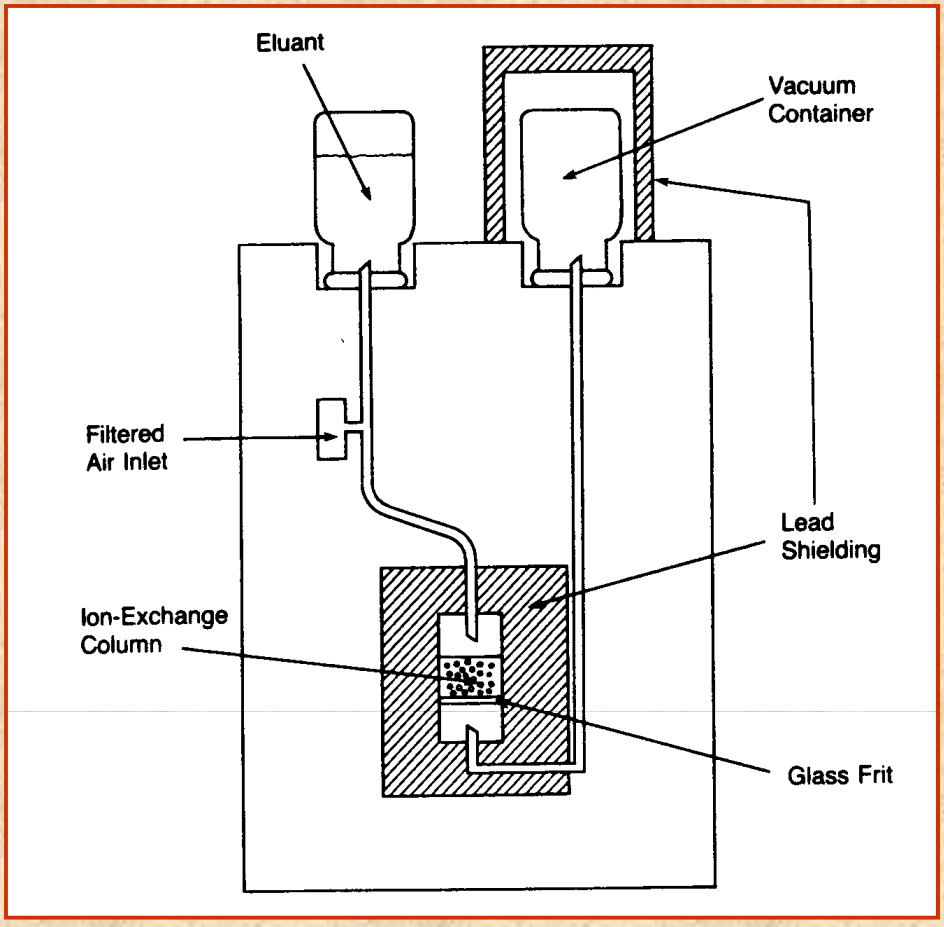
C-11, N-13, O-15, F-18

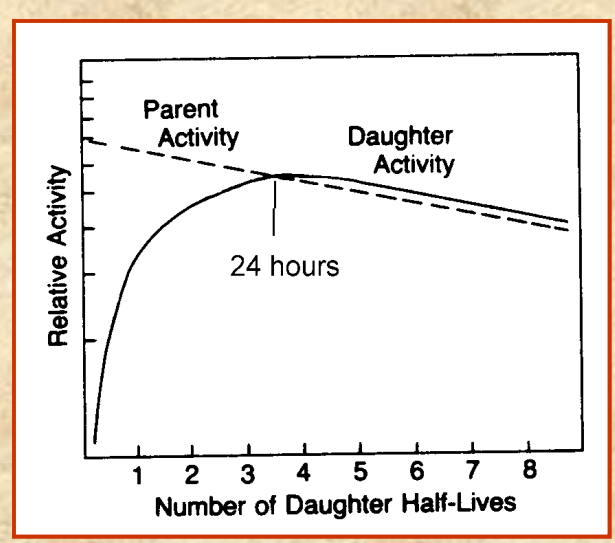
Cyclotron Center





Transient Equilibrium





A GENERATOR is a device with:

- A long lived parent which decays to a short lived daughter
- A process by which the daughter can be chemically separated from the parent = Elution
- A consistent yield of daughter radionuclide
- A relatively long shelf life which is determined by the parent radionuclide

CHARACTERISTICS OF THE 99-Mo/99m-Tc GENERATOR

- Parent radionuclide Molybdenum-99, produced by the fission of U-235, is absorbed onto an alumina column
- Daughter radionuclide Technetium-99m, by-product of the decay of Mo-99, is eluted off the aluminum molybdate column using saline
- The calibrated activity on the generator is due to Mo-99 and ranges from 1-16 Ci
- Shelf life of about one week due to 67 hour half-life of Mo-99 not the 6 hour pT 1/2 of Tc-99m
- It takes 24 hours, four daughter half-lives, for maximum build-up. If you wait 6 hours after thelast elution, you could only get 50% of the calibrated activity.

PROCESS OF ELUTING A "DRY" Mo-99/Tc-99m GENERATOR

("Dry" meaning that the saline is not included in the generator)

1. Obtain a vial of saline and an evacuated vial with a vacuum slightly higher than the volume of the saline vial.
2. Swab the septum of the saline vial with 70% isopropyl alcohol
3. Remove the shipping vial and attach the saline vial to the inlet needle on the generator
4. Place the evacuated vial in a vial shield
5. Swab the septum of the evacuated vial
6. Remove the shipping vial and attach the evacuated vial to the outlet needle
7. Wait 1-5 minutes
8. Remove the ^{99m}Tc04 eluate from the outlet needle and replace it with the shipping vial
9. Remove the empty saline vial and replace it with the shipping vial

Assay the eluate to determine the activity of ^{99m}Tc04, sodium pertechnetate.

Divide activity by volume = activity concentration

ACTIVITY OVER TIME

Final activity = original activity x decay factor

$$A = A_o \times df$$

(decay factor = $0.5^{\text{elapsed time/pT}}$)

Example: If the activity concentration at 8:00 am was 246 mCi/ml, what would it be at 10:00 am

$A = 246 \times 0.5^{2/6}$

$A = 246 \times 0.5^{0.333}$

$A = 246 \times 0.794$

$A = 195$ mCi/ml @ 11:00 am

If you need 150 mCi of ^{99m}Tc04 to make-up an MDP kit, what volume of ^{99m}Tc04 do you need?

$$\text{volume} = \frac{\text{activity needed}}{\text{activity concentration}}$$

$V = 150 \text{ mCi} / 195 \text{ mCi/ml}$

$V = 0.78$ ml

You would then need to QS to volume to 3 ml by adding

2.22 ml of saline. Now the activity concentration is 150 mCi/3 ml = 50 mCi/ml

CHARACTERISTICS OF SPECIFIC RADIOPHARMACEUTICALS

OBJECTIVES:

1. List the radiopharmaceuticals used in nuclear medicine.
2. Identify the clinical use of each radiopharmaceutical.
3. Identify the physical half-life and imaging energy of each radiopharmaceutical.
4. Identify the normal adult dose/dose range for each radiopharmaceutical.
5. Explain at least one other characteristic of each radiopharmaceutical.

- Radiopharmaceuticals localize in organs because of the function of the organs
- Normal function = uniform distribution
- If there is poor function, there will be little uptake and so little or no activity = "Cold" spot or area
- If there is hyperfunction, increased blood flow or abnormally high cellular activity, there will be higher uptake and higher activity = "Hot" spot

QUALITY CONTROL OF RADIOPHARMACEUTICALS

OBJECTIVES:

1. Define radionuclidic purity.
2. Identify the radionuclidic impurity we have to test for in the ^{99m}Tc04 eluate.
3. Describe the test used to assess radionuclidic purity.
4. Define chemical purity.
5. Identify the major chemical impurity.
6. Describe the test to determine chemical purity.
7. Define radiochemical purity.
8. Identify the two possible radiochemical impurities.
9. Describe the test used to assess radiochemical purity.
10. Identify the particle size limits for ^{99m}Tc-MAA.

QUALITY ASSURANCE TEST ARE DONE TO INSURE THAT THE RADIOPHARMACEUTICALS ARE SAFE FOR PATIENTS AND DO NOT ADD UNNECESSARY RADIATION DOSAGE.

RADIONUCLIDIC PURITY

- the activity in a radiopharmaceutical due to the desired radionuclide
- Molybdenum-99 in the ^{99m}Tc04 eluate is a radionuclidic impurity
- 10 CFR: 35.204 Permissible Molybdenum-99 Concentration = no more than 0.15 uCi of Mo-99 per mCi of Tc-99m
- The presence of Mo-99 increases the radiation dose because of the higher energy and longer half-life
- A "Moly Breakthrough" test is done to assess the level of Mo-99

1. Assay the ^{99m}Tc04 to determine the mCi
2. Assay the empty "Moly" Shield
3. Place the eluate vial in the "Moly" shield
4. Assay the vial in the shield on Mo-99 settings to determine the uCi
5. Divide the uCi of Mo-99 by the mCi of Tc-99m

CHEMICAL PURITY

- the amount of the ^{99m}Tc04 in the correct chemical form

- Alumina is a possible chemical contaminant

- The USP XXII limit = the alumina content must be less than 10 ugm/ml of ^{99m}Tc04

- Alumina content colorimetric assay

  1 Obtain an indicator strip

  2 Drop a small drop of the eluate on the indicator strip

  3 Drop a small drop of the 10 ugm standard

  4 Compare the color of the eluate with the standard

  If the color is lighter the alumina content is less than 10 ugm/ml

- Too much alumina can cause flocculation in phosphates radiopharmaceuticals and clumping in particulates

RADIOCHEMICAL PURITY

- The fraction of the activity due to the radiopharmaceutical in the correct chemical form
- Free pertechnetate and hydrolyzed reduced pertechnetate are possible radiochemical contaminants
- The most common test is radiochromatography
- Radiochromatography uses the migration of a solvent up a support to separate out different components
  - solvents = saline an aqueous solvent
  - acetone an organic solvent
  - among others
  - supports = Instant Thin Layer Chromatography(ITLC)
  - Whatman paper
- Usually the aqueous solvent is used to identify the presence of the impurities.
- The migration of the solvent on the support is measured in relative flow(Rf) values ranging from 0 at the origin to 1 at the solvent front.

RADIOCHROMATOGRAPHY PROCEDURE

1. Pour the desired solvent into a developing chamber.
2. Mark the origin on an ITLC strip
3. Place a small drop of the radiopharmaceutical at the origin.
4. Place the ITLC strip in the developing chamber
5. Allow the solvent to migrate almost to the end of the support.
6. Use tweezers to remove the strip from the chamber.
7. Allow the strip to dry.
8. Check a relative flow chart of radiopharmaceutical to see where the impurities are in relation to the origin.
9. Cut the strip accordingly.
10. Count both halves, one part will represent the impurity and the other will be the RAPH
11. Divide the impurity count by the total counts on both halves and multiply by 100 to get the percentage of impurity. Subtract the impurity from 100 to get the purity percentage.

The maximum acceptable particle size, USP, for ^{99m}Tc-MAA is 150 microns, most will be 30-90 microns

- Check particle size with a hemocytometer and a light microscope
- No single particle should be larger than three squares on the hemocytometer, each sq.=50 microns