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## **ASHP USP 797 Symposium June 200**

### **ASHP Summer Meeting Boston, June, 2005**

#### **1. USP Seminar...."General chapter 797 and More", Sunday, June 12**

This session was not part of the meeting. Speaker was Loyd Allen, Ph.D.....This guy does a lot of work with the USP in the area of compounding. Also is the editor of the International Journal of Pharmaceutical Compounding, so it is not surprising that he spent a lot of time on USP 795 that deals with nonsterile compounding and not on 797. Still interesting, but not what the title of the session indicated.

Changes to the USP 797 chapter that will take place in January 2006. Note that the USP is now updated each year. New edition comes out in January of each year.

1. The biggest change is that 797 does NOT apply to preparations that are given within 1 hour and which have been fully administered within 12 hours. This is for 3 ingredients or less (low risk). Note that in other sessions there was talk that the 12-hour exemption would not be part of the new standard. Time will tell.
2. Beyond use dating (BUD) for refrigerated, medium risk items will go from 7 to 9 days.
3. The buffer area will go from ISO 8 to ISO 7; the ante area to ISO 8.
4. SDV must be used within one hour if conditions are greater than ISO 5, but can be used for 6 hours under ISO 5 conditions.
5. MDV will go from BUD of 30 days to 28 days
6. Surface sampling will be needed monthly for our volume (> 300 preparations per week). This is where open plates are used to test for surface contamination of the air. Need to learn more about this.
7. Isopropyl alcohol will no longer need to be sterile.
8. Gowning procedures will change....easier.

A lot of 797 has to do with documenting what we do in the preparation of sterile products: Policies and procedures; education and training; cleaning; testing of equipment, etc. must all be documented.

The International Journal of Pharmaceutical Compounding is a good place to look for cleanroom design information. Get references from Dr. Allen at [lallen@ijpo.com](mailto:lallen@ijpo.com). He welcomed email questions.

Allen noted that the syringes we use for compounding should be tested (by lot) to make sure they are accurate. Good idea for 1 and 3ml syringes. Weigh the syringe, then pull up 1 ml of water....should weight one gram more.

USP's authority came from the 1938 Pure Food and Cosmetic Act which gave this private, nonprofit organization authority to determine drug standards. They do not enforce, just set standards for the FDA and Boards of Pharmacy to enforce.

In the 1990s the FDA became very concerned about pharmacist compounding activities. They concluded that all compounded products were new drugs and as a result needed to go through the FDA approval process. This effectively would have shut down compounding. FDA applied their new standard sparingly, but did create a problem for some compounders.

Then in 1997, The Food and Drug Act Modernization Act changed all that by allowing compounding by pharmacists of patient specific preparations. However, this law was thrown out by the courts in 2001 after some pharmacists brought suit because of the acts ban on advertising. The FDA can now require compounded drugs to comply with new drug standards. Again, they are applying this standard sparingly (i.e., selective enforcement).

Over the years the USP has gotten away from its early roll of setting standards for compounding. In the 20<sup>th</sup> century changed to supporting manufacturing of drugs and not the pharmacist. That is changing now. With 795 (nonsterile) and 797 (sterile) standards, the USP is now defining how compounding needs to be done. The Boards of Pharmacy will enforce these rules. Both these chapters will also have monographs on common preparations...very good idea. There are about 100 monographs now and the number will certainly increase. These have stability data supplied by USP scientists.

The FDA wants compounding pharmacists to be accredited and certified since little is now taught in schools of pharmacy. There is now a Pharmacy Compounding Accreditation Board which is supported by the APhA and numerous other professional groups. They will start accrediting soon. Good move.

Note that the USP defines beyond use dating and expirations differently. The latter is for manufacturers that follow GMPs. The former are from compounders (i.e., pharmacists). Generally, beyond use dating should not go over 6 months for nonsterile preparations.

Cleanrooms.com is a good source of information on equipment.

We need to get a black and white background field for checking IVs. Part of standard. Maybe we need to set up a station to do this. Clean Air Technology has one of these for about \$300.

The media fill test that we are doing is not good enough for medium risk products. Need to check on this and see if there are media fill kits for medium risk products. The media fill test for medium risk involves the transfer if larger volumes and more transfers.

Need to do these yearly for low and medium risk. More frequent for high risk. Don't have to use the USP method, but whatever is used, must be just as good.

Isolation chambers...Allen thought that if you did more than 10 to 15 sterile preps per day, then they were too cumbersome. Other speakers thought they were OK for medium volumes.

Need to have staff read the department's sterile product P&P each year and to sign off on them. Part of training documentation.

What the buffer area (i.e., cleanroom) must have..

- Seamless floor which runs up the wall 4 to 6 inches

- Walls sealed (epoxy coated)

- Ceiling tile sealed (epoxy coated)...can get ceiling tile that will do this, but need to caulk and use double stick material to seal against ceiling grid of suspended ceiling.

- Light fixtures are a problem...also must be caulked.

- Cabinets need to run to the ceiling...don't have anything that can collect dust.

- No sinks and drains in the buffer area

- Note that no wall is needed between the buffer area and the cleanroom for low and medium risk products. Airflow goes from buffer to ante area.

- Pre-made cleanrooms are available which run about \$30K

With no sterility testing...

Low risk...48 hours at RT, 14 days if refrigerated and 45 days frozen

Medium risk...30 hours, 7 (soon to be 9), 45 days

High risk...24 hours, 3 days and 45 days

Dr. Allen spent a bit too much time on 795, but there was a lot of stuff in 795 that applied to 797. He should be a good source of information on this topic. He invited emails.

## **2. June 13, 2005, Morning session on 797...Environmental Monitoring, Infection Control and Validation Testing.**

This concerning environmental testing as well as process testing. Quite good. The speaker was Eric Kastango who has a consulting business in this area.

He stressed the importance of leadership in getting compliance from staff. If you believe this is important, the staff will usually make it a priority.

Isopropyl alcohol...mentioned that sterile alcohol is no longer needed (will be adopted as of 1/06). The reason this was an issue is that IPA is a very poor germicide when it

comes to spores and fungi. If these are a problem, need to use some other type of disinfectant. Don't rely totally on IPA.

Areas used to prepare sterile products are not self-cleaning. They need to be frequently cleaned to ensure the lowest possible bioburden in the area. We can't sterilize these areas, but we can make them as clean and germ free as possible.

Areas used to prepare sterile products should be cleaned just like the OR is. Find out what is done in that area and get Environmental Services (i.e., housekeeping) to do the same for the pharmacy.

Need dedicated equipment for cleaning the cleanroom (e.g., mops, buckets, etc).

Need sealed surfaces which resist the effects of deep cleaning. Many agents used to clean these areas are quite corrosive. Need to get a special stainless that is less subject to pitting by these agents.

Need to document cleaning process and have a clear procedure for all cleaning that must be done.....just like we do for the hoods now, but for the whole IV prep area.

Make the cleanroom as spartan as possible to make it easier to clean. Don't have a lot of stuff in this area that will collect dust.

Stressed the importance of particle counts. Microbes don't fly! But they do hitch a ride on airborne particles. These particles are not in themselves infectious, but they help microbes move into areas where sterile products are found. Thus, it is very important to reduce particle levels to as low as possible.

Need to get nonviable particle counts from the guy the checks our hoods. This needs to be one every 6 months.

Also need to test for viable particles...microbes. This is done by air and surface testing. For low/medium risk preparations, need to do air sampling at least monthly. Should have no growth in the hood (critical area), but will see some counts from the buffer and ante-room areas.

Also need to test surfaces and finger tips....for our volume probably every 3 months. Use sterile swabs for counter testing and agar contact plates for finger testing. Actually touch fingers (in gloves) to surface of agar and then incubate to determine the level of contamination.

Environmental monitoring gives one a good indication about how well things are working. How well cleaning is done; how well the air conditioning is working; how well the hoods are filtering air, etc. Need to test on a regular basis to determine a baseline. Then need a plan of action of results indicate a problem.

Air testing can be passive....just expose a plate for 1 to 4 hours and then incubate. Or can use active sampling. These instruments pull in air (40 liters in 4 minutes) and deposit particles on an agar nutrient strip. These cost a lot...\$3500 for an inexpensive model. He suggests doing both passive and active. These critical areas, buffer areas and ante-room. The guy that checks our hood may be able to do the active testing for us. There are numerous sources for the passive plates. Incubate at 30-35 degrees C for 48 to 72 hours and count colonies. Note that settling plates have a raised area. Finger tip plates look like normal plates.

See the June 15 issue of ASHP for details on how to do environmental testing.

One interesting fact....even after washing, on average, skin has 20,000 microbes per square mm of skin.

Need to develop a procedure for testing....where to test, how to test, how often to test. Then follow procedure and look for trends.

See USP 1116 for information on how many colonies are acceptable.

Process verification is also needed. This is a test of personnel to see if they can do the processes involved in sterile product preparation without contamination. Use tryptic soy broth in preparing TPNs for example. Use this broth in place of AA and or dextrose solution. This guy said that TPN is not a very good growth medium...too hypertonic.

MD Anderson did some testing like this and found that 5.2% of the tests were positive for contamination. Reduced to 0.3% by using gloves and frequent cleansing of gloves with IPA.

Incubate these tests for 14 days at 25 degrees or 7 days at 25 and then 7 days higher. Turbidity only results if have over a million organisms growing per ml. Look for floaters too. Some fungi don't result in turbidity...get clumps instead.

Conduct these tests under the worst case scenario.....i.e., end of a busy day.

Testing employees involves three types of tests....didactic (written test), motor skills (check list) and media fill process verification using a procedure that is similar to the most complex products made in the pharmacy (for us medium risk). Ideally, one would have employees take validation tests for all types of products prepared. TPN and PCA would probably be good for us.

Check your filters to make sure they specifically say they can be used for sterilization and that they pass the USP tests for filter sterilization. Some filters are not meant for sterilization.

See the handout for a list of companies that provide testing media (bioMerieux, Valiteq, Millipore, QI Medical). Be careful of the source of this stuff. Some media has been

found to be a poor growth medium! Test these media to make sure they work. Buy from a reliable source.

Good presentation.

### **3. June 13, 2005, Afternoon 797 session 1: Facility and Equipment**

The speaker was Jim Wagner....Consultant in the area of critical environments for both drug processing as well as hazardous materials handling.

Pretty good speaker, but the acoustics of the hall made it hard to hear.

Talked a fair amount about barrier isolators. There are two types of airflow...turbulent and unidirectional (laminar) used in isolators. Most companies use the latter. MIC uses turbulent. The guy from MIC claims that all barrier isolators are turbulent; Jim Wagner thinks differently. He claims that he's tested a number of the barrier isolators and some do in fact have unidirectional flow. The placement of the exhaust vents is very important in the design of the unidirectional flow models. Flow is from top to bottom. In the turbulent flow, flow is from one side (top) of the hood to the other side (top).

Talked a bit about HEPA filters. Usual standard is based on 0.3 micron filter size. Should be able to trap at least 99.97% of this size particle. Noted that HEPA will not trap nonparticulate matter....gases, vapors for example. Thus can't be expected to stop toxic vapors. This is a growing concern with some chemo. Need to check MSDS sheets for all our chemo to make sure none are volatile.

Need to specify the quality of HEPA filter in designing a cleanroom. Best to use type C. This type is tested for leaks and traps 99.99% of 0.3 micron particles. Type A traps 99.97%, but is not tested as well as Type C. Types D and E are overkill for our application.

The hood must be ISO 5 (old class 100) and the buffer (cleanroom) must be ISO 7. It is ISO 8 now, but this will change January 1 with the revision of 797. Ante-areas must be ISO 8. So it goes from 100 to 10,000 to 100,000 particles. For particle counts the standard is 0.5 micron particle size.

Note that laminar flow hoods offer product protection only. They do not provide protection to personnel from toxic vapors. The approximate flow rate in a hood is about 90 feet per minute.

Barrier isolators are fairly new to the US although they have been used in Europe much longer. Note that in Europe, barrier isolators are in cleanrooms. At present there is little data to justify not having them in cleanrooms. The manufacturers of barrier isolators are certainly trying to prove they can be used outside of cleanrooms. New USP standard will leave it up to the manufacturers to prove they can be used without a

cleanroom. The current USP standard states that it is preferred that barrier isolators be kept in cleanrooms...does not require.

One of the big concerns about barrier isolators is how one gets materials into the working chamber without bringing in a lot of particulate contamination. Need to have HEPA filtered air into the pass through chamber so that particulates can be flushed out. Need to think through carefully as to how one would get materials into the antechamber and then into the working chamber without a lot of crap coming in with it. Need a good-sized antechamber to remove wrappers, etc. before the materials are passed into the other chamber. Note that the MIC brand of barrier isolators does not use filtered air to flush out the antechamber.

For most work, the chamber should have a positive pressure. Most models can be either positive or negative pressure, but can't switch from one to the other. For chemo want a negative pressure.

Cleaning is also an issue with barrier isolators. Sometimes corners and grills are hard to reach and clean. There are tools available for this type of cleaning, but the ease of cleaning needs to be a consideration in selecting a barrier isolator.

Talked some about NIOSH standards. Need to review these standards. When sterility and protection from hazardous materials is important, the recommendation is for Class II type B2, Class III BSC (Biological Safety Cabinet) and Aseptic Containment Isolators. The B2 does not re-circulate the air from the hood. The type B2 hood has no re-circulation and that gets rid of any vapors, but is expensive to operate. Barrier isolators that are used for chemo have a negative pressure. Should be externally vented.

NIOSH also wants the chemo hood and regular hood in separate areas. Speaker thinks this is a good idea. Need to further explore this.

Can use Class II type A2 (what we have) or Class II type B1 for toxic drugs which are not volatile. These have some recirculation and the HEPA filter can be expected to stop particulate toxic material. All Class II cabinets have an open front. Differ as to how the air is handled after leaving the work area....totally exhausted, partially exhausted or totally re-circulated.

NIOSH now wants chemohood exhausted. Check this out and determine what kind of vertical flow hood we have for chemo (Class II, type A). Make sure the exit for our chemo hood is not near any intake for the hospital. Question for Engineering.

All hoods (vertical and horizontal) should have a monitoring gauge....use flow, not pressure.

All items going into the cleanroom must be wiped down. See 797 for an example of the procedure that should be used.

Need a place to gown that isn't too crowded. Also plenty of room to degown in anteroom.

Don't need a wall separating the buffer area and the anteroom. Can have a line of demarcation or can have the floor a different color in the buffer area. Note that carts that are in the buffer area never go into the anteroom and vice versa. Have two carts. Transfer between them. Can wear shoes in the anteroom, but booties must be worn in the buffer area.

Airflow in the buffer area (i.e., the cleanroom) is not laminar flow. The air is filtered to remove particles and the flow (30 air changes per hour) removes particulate matter down to the required level. The air coming into the buffer area must be filtered through HEPA filters. Flow is usually from the ceiling down to vents along the lower wall near the floor. Should have inflow filters throughout the cleanroom. Avoid turbulence near the hood. Don't want too high a flow of air in the buffer area...can cause problems with the hood flow. Flow goes from the cleanest to dirtiest part of the area (from buffer to anteroom).

Temperature control is very important in the cleanroom. All the garbing makes for hot work. Must also control humidity.

Must know the properties of the hoods prior to designing the cleanroom!

This guy knows his stuff.

#### **4. June 13, 2005, Afternoon program 2: Budgeting for and Designing a Cleanroom**

Kate Douglas...RN that has done a lot of work in the sterile compounding and homecare area. Has built four cleanroom facilities. Seems to be knowledgeable.

Focus was on practical aspects of cleanroom design.

Thinks the air temp goal in a cleanroom should be about 66 degrees +/- 4 degrees.

Need to clean the back of the hood too...keep away from the wall.

Typical cost for a cleanroom is \$190 to \$220 per square foot.

Normally have a suspended ceiling with a grid and the usual drop-in tiles. But must use silicone to seal the ceiling tiles to the grid. Us epoxy surface sealed tiles so they can be easily cleaned. Make sure the tiles are sealed before signing off on the job. This is often the last thing to be done and can be overlooked.

Use continuous floor covering that has heat sealed seams. Not gaps or crevices for microbes to grow in. Coving up the wall 4 to 6 inches. Everything sealed. No floor drains or sinks in the buffer area.

Usually the pressure difference is 0.05 from cleanroom to anteroom.

Don't want too high a pressure difference....can cause problems with doors.

Pass through that have doors on either side work well....for example double sided refrigerators.

Lighting should be sealed too. Need plenty of light. Need to be able to change bulbs from inside the room.

No sink in the cleanroom. Need some provision for any eye wash, but doesn't need to be part of sink. Need a knee control for the faucet on the sink.

Avoid hand dryers...slow and break down. Expensive. Use lint free towels.

Use cleanroom stainless steel. This avoids pitting from constant cleaning.

When buying furniture (carts, etc), make sure to think about how easy it will be to clean. Cleaning is done frequently.

Should put plenty of electrical plugs and computer plugs in the cleanroom even if you don't need them today....for future use.

She likes laminar flow work benches rather than hoods. Laminar flow air comes from above and flows down on the work counter and out exhaust vents low on the wall. Lexan shields coming down from the ceiling (down about 3 feet and about 3-4 feet from the wall) keep the laminar flow air directed over the bench. These are not the usual design and need a lot of testing to make sure they work as they are designed. Advantage is a larger and more flexible work surface.

She mentioned several times that oxytocin is now considered hazardous by NIOSH. I guess we will have to prepare oxytocin bags in the vertical flow hood from now on. What about all the waste....dispose of like chemo?

She too was not sold on barrier isolators. She thought they should be in ISO 8 rooms or better unless manufacturer can demonstrate otherwise.

Put a telephone in the room. That way if a person gets a call, they don't have to ungarb and come out.

OK presentation

## **5. June 14, 2005, Morning session: Drug Stability, Storage and Beyond-Use Dating.**

Patricia Kienle...Cardinal. Very good presentation.

The presentation focused on developing policies and procedures for sterile product preparation and quality control procedures.

Need to look at all areas of the hospital to see where sterile products are made. For example how are ophthalmic preps made in the OR? How is tobramycin bone cement made? How are epidurals made in the OR and L&D? Also need to make sure preparations made elsewhere (i.e., outside of the hospital) are not making their way into the hospital.

Sterility problems with sterile preparations made by pharmacists (and other practitioners) have been known for years. Not much changed before 797. Many knew there was a problem, but few did anything about it.

She noted a couple of times in her presentation that many high-risk agents should not be made. Need to examine what is made in this category and outsource or stop as much as possible. Most pharmacies are not equipped to make sterile high-risk preparations in a reliable manner.

Immediate use exception will be changed in January 2006. Meeting of USP takes place in early July, 2005...will know after that. They will probably exempt products that are used within 1 hour of preparation, but may delete the 12 hour exemption (i.e., administered within 12 hours) since 797 does not speak to administration elsewhere. The JCAHO also exempts CSPs (compounded sterile preparations) that are used with no intervening steps. Good definition. Noted also that vial/bag systems like ADDvantage are also exempt. USP 797 deals with the preparation and storage of sterile preps, not those for immediate use.

If other areas, like the OR, made preps for later use, must comply with 797 standards.

JCAHO and 797 require a formal QA plan. JCAHO implementation schedule gives until July for such a plan, but 797 requires it now....this is the standard we must follow. If anything goes wrong and the standard has not been followed, legal problems could result. Several states have started to enforce 797.

Need a formal QC plan that includes monitoring and follow-ups. Speaker suggested appointing someone else to do this stuff...a pharmacist or tech that can be in charge of sterile preparation in the pharmacy.

The QC plan needs to be short and concise....don't write something so extensive it cannot be followed.

Facilities must be monitored...hood (iso 5), buffer/cleanroom area (iso 7) and anteroom (iso 8). Need to be able to show, through environmental monitoring, that these areas have particle counts that are in line with these standards. Need to do this at least every 6 months for an area to compounds low/medium risk preparations.

Mention was made again of the NIOSH standards. These were published last September and define how cytotoxic drugs must be prepared. These are advisory standards, but where employee safety is concerned, they need to be followed. Need to have a separate room with an exhausted hood for these drugs. Get the list (see on-line reference in handout) that lists the drugs....oxytocin is on the list. What else?

Need to also monitor air, surfaces and fingertips for microbial contamination. There is a standard for how often this needs to be done. Based on volume of CSPs made.

Central Supply people can be a great source of information about sterilization and QC procedures to maintain good infection control. Also see what they do in the OR to monitor that area for microbial burden.

New for 797 is the media fill requirement for employee testing. Need to be doing this now, regardless of the facilities you have. Must do this at the level of what you prepare.....we need to use the TPN level. May also need one for PCA syringes. Test employees yearly for low and medium risk. Document everything. Employees also need to take a yearly written test and be observed for technique. Also need to review P&P and sign off that they have read it,

Need written P&P (SOPs) for everything that we do in the preparation of sterile products. Need to be up-to-date and be used by employees.

Need to get one of those black and white boards for checking CSP for particles....set up a checking station or two where IVs are checked.

Sterility testing for low and medium risk products is not necessary unless one exceeds to beyond use dating beyond what USP 797 specifies. If you do need to do sterility testing, check chapter 71 of the USP.

See the list of topics that should be covered in P&P...page 8 of the handout.

Get infection control involved in all of this. In fact, results of monitoring should be reported to the Infection Control Committee rather than P&T. The Infection Control nurse should know a lot about 797....has been a hot topic in that area. Great resource on hand washing and other topics. They are now concerned with the OR and Central Supply...need to add the pharmacy IV prep area to that list.

Need to do a GAP analysis....see the ASHP website.

The QC plan should include what will be done when something odd happens (e.g., the particle counts are out of spec for a given area or someone fails their media fill test. What will be done?).

After the July USP meeting check Google for the approved changes.

Cleaning procedures need to be defined in some detail. Already do this for the hood. Now need to do it for the floor and other surfaces. Shelves need to be cleaned much more frequently. Probably need to get rid of some of this stuff in our IV area. Need a dedicated person from Environmental Services to clean this area....like the OR.

Nails can only be ¼ “ long....CDC requirement. No makeup. See what they do in the OR and Central Supply regarding makeup and follow that lead. Use the infection control nurse as a resource for this issue.

There is a middle area...between exempt and 797 that is not defined as yet. For example, what beyond use dating is allowed for hoods outside of a cleanroom?

P&P needs to speak to reusing IVs. Need to review how they are stored after leaving the pharmacy. Can one justify reusing them?

Excellent presentation.

## **6. June 14, 2005, Afternoon session 1: Drug Stability and Beyond Use Dating**

The first presentation was by Larry Trissel....needless to say he knows his stuff and has had a big impact on 797.

He talked a bit about how the standards were determined. They really tried to focus on patient safety. Note that the committee that defined 797 was made up totally of pharmacists. He noted that the standards apply to all pre-administration manipulations of sterile products. It also applies to all personnel involved, regardless of their profession (i.e., nurses and physicians too).

One of the responsibilities of 797 (there are 13) is to determine beyond use dating. This is the term used for “expiration dating” for compounded preparations. Officially, expiration dating is only used for products which are manufactured, not compounded. These terms have legal significance in these USP standards. It is the responsibility of the pharmacist to determine the beyond use dating for any product made under his or her direction. Literature data should be used if there is no direct stability testing. The USP also provides some guidelines when literature data do not exist.

Basically, beyond use dating results from considering two factors for a given preparation. First, the chemical stability and second the microbial contamination risk. The former is old hat, so to speak. In the past we have assumed that a product was sterile and just considered chemical stability. However, with 797, we now acknowledge

that some of the sterile products we make are contaminated. So if they are contaminated, how long can they be used before the contamination becomes a problem.

The assumption that contamination may be present is different than the situation with a manufactured product. Here, due to all the testing that is done, one can assume the product is sterile. So expiration dates are based mainly on chemical stability. Not true for CSPs...not enough testing to justify that assumption.

Beyond use dating starts at the end of compounding and ends at the start of administration. He acknowledged that the standard does not tell us everything. For example, the length of time something can hang, is not addressed. This is a professional decision. For example, if something has a 24 hour beyond use date, that means that it can be hung at hour 24. But can it be administered over 1 hour or 12 hours....not defined.

He noted that one million organisms per cc produces turbidity. Fewer organisms are hard to see. So something can look really good and still have a lot of contamination.

The only difference between low and medium risk preparations is that the latter require more complex manipulation. More steps, more ingredients, more time....all could bring the compound into the medium risk category.

Larry noted that at MD Anderson, their first employee testing using media fill had a 5.2% failure rate. After starting to wear gloves and using IPA to clean gloves frequently, the rate went down to 0.3%.

Do a Google on "Valiteq" process.... They have a 10 step media fill process that we might be able to use to simulate a TPN preparation.

He thinks we should not make high risk products. Too much risk to the patient. Leave this up to the companies...they can do it better. High risk preparations are unsafe!

In the absence of specific beyond use recommendations, the USP has some guidelines for chemical stability. These are in chapter 795.

Solids and non-aqueous liquids...25% of remaining expiration date or 6 months whichever is shorter.

USP bulk substance...not more than 6 months

Aqueous formulations, 14 days refrigerated

All others not more than 30 days or the intended duration of therapy, whichever is shorter.

Note that these are for chemical stability only.

When the possibility of microbiological contamination is taken into consideration, then the beyond use dates are:

Low risk...48 hours room temp, 14 days refrig, 45 days frozen

Medium risk...30 hours, 7 days, 45 days

High risk...24 hours, 3 days, 45 days

Note that lipids are NOT included in these recommendations. Lipids at RT are 12 hours. This includes intralipids and propofol. Check on the latter and make sure it is not being drawn up ahead of time in the OR.

Need to spell out the details of beyond use dating in P&P. It should be clear how beyond use dating is determined.

This was a good talk. Well presented.

## **7. June 14, 2005, Afternoon session 2: New Technology**

The next talk was presented by Bernadette Ellegard. She covered this compounding device (Gri-fill) which I had no interest in. Why they included such detailed info on this product, I'm not sure. This machine can be used to prepare CSP in large quantities and with longer beyond use dating that allowed by the USP. Only of use in very large pharmacies.

## **8. June 14, 2005, Afternoon session 3: Chemo Preparation and Contamination**

Jim Jorgenson from Utah presented some work he has done with chemo contamination in the pharmacy at the University of Utah Hospitals and the use of PhaSeal containment devices.

He went over some of the work that had been done in the past to show that chemo contamination ends up in the pharmacy and in personnel. OSHA has a list of compounds that are human carcinogens or are suspected as being so...about 30 chemo drugs are on this list. Need to get the list from Jorgenson.

Also went over data that relates low levels of chemo to injury. None of the data is very good, but it is impossible to test this sort of thing. There is a retrospective study that shows an increased risk of abortion or stillbirth in women that handled chemo while pregnant. Also a study that showed Danish chemo nurses had a higher incidence of leukemia. All this is somewhat; indirect, but makes one have concern.

Jorgenson tested their pharmacy and staff at Utah and found contamination everywhere. After are now using the PhaSeal product and contamination has dropped both in the area and in the staff.

He felt that some vials of chemo had contamination on them from the manufacturer. Keeps his drugs in a separate, well ventilated, area. Should not remove vials from their box prior to being made.

The cost of PhaSeal is pretty high...\$10 to 15 from start of prep to finishing admin. Works to contain the drug both in the pharmacy and the clinic during administration. Using PhaSeal really reduced surface and personnel contamination.

Can all these problems be solved with a barrier isolator? No. Jorgenson felt that one would just contaminate the barrier isolator and eventually everything else without PhaSeal. Both MD Anderson and Utah continue to use PhaSeal.

#### **9. June 15, 2005, Morning sessions: Training**

I did not attend these sessions.