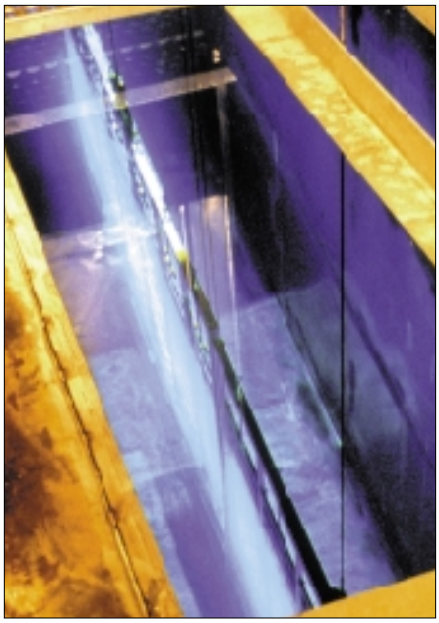
Inside a gamma sterilizer



Gamma radiation has been recognized since the 1950s as a safe and effective method of sterilizing medical products. NN *toured a gamma radiation sterilization facility to find out why.*

BY PATRICK SINCO

Above right: The radiant source rack, at rest in an approximately 20-ft-deep shielding pool, houses about 550 Co-60 pencils. **Above:** SteriGenics' radiation sterilization facility in Gurnee, Ill., covers 80 000 sq. ft. (Photos courtesy of SteriGenics International, Inc.)

THE PROCESS ITSELF is simple enough. A manufacturer drops off a load of boxes containing, say, cleanroom towels at the "unprocessed" side of the warehouse. The boxes are loaded onto a conveyor system that slides them past a cobalt-60 source. They are unloaded and placed on the "processed" side. The manufacturer picks them up—the boxes are even in the same order as when they arrived. It takes about five days—or about half the time it would take to sterilize those towels using the other popular method of medical sterilization, ethylene oxide (EtO) gas fumigation.

The simplicity and speed of gamma radiation sterilization is a great part of its appeal for sterilizing health care products, components, and packaging. And it is a significant reason that gamma's share of the sterilization marketplace is expected to increase by the end of 1999 from 1994, and EtO's decrease, according to an article in the September 1997 issue of *Medical Device & Diagnostic Industry* summarizing an in-house study of industrial sterilization trends conducted by DuPont Co.

The gains may be slight—gamma's marketshare is expected to grow to 49 percent from 47 percent, and EtO's to shrink from 46 percent to 44 percent. But the gap between the two may widen if the market for industrial sterilization continues to expand in the coming years as vigorously as the growth that the study predicted will occur between 1994 and 1999—a more than 25 percent increase in cubic feet of sterilized product. Twenty-one years ago, EtO comprised 95 percent of the sterilization market for medical devices.

EtO offers its advantages: It has the inertia of half a century behind it; the gas is cheap; it is compatible with some materials and pharmaceuticals that radiation is not. It is most effective, however, at destroying microorganisms on the surface of products and has difficulty permeating sealed chambers; gamma radiation is deeply penetrating. The vacuum and pressure requirements of EtO processing can work to undermine the integrity of the packaging seal, jeopardizing the product's sterility; gamma radiation has little to no effect on packaging. The EtO process leaves a residue on the product and requires an aeration period to allow the gas to dissipate to levels that are safe for human handling; gamma-irradiated product is good to go straight from the cell. EtO requires rigid control of variable parameters such as temperature, pressure, humidity, and gas concentration; the principal processing variable with gamma is time. EtO is complicated; gamma is simple.

The person to whom gamma sterilization is not so simple, however, is the general manager of a gamma radiation sterilization facility, where those trucks bring their loads of lab sponges, surgical kits, specimen containers, cleanroom garments, orthopedic implants, and other medical products that need to achieve sterility levels that amount to one microorganism in a million. The more than 4 000 000

curies in the Co-60 source rack that does just that at SteriGenics International, Inc.'s Gurnee, Ill., facility are the responsibility of General Manager Tony Valentyn. He and David Meyer, president of the company's Medical Sterilization Division, showed *Nuclear News* around the facility and detailed the work process involved.

The rigors of scheduling

The contract radiation sterilizer's responsibility boils down to delivering a specific dose—or, actually, a dose that falls within a range specified by the product's manufacturer. It is the manufacturer's responsibility to determine the maximum and minimum dose. The minimum dose will need to achieve the product's sterility assurance level, or proper biological reduction. The maximum dose is calculated to prevent adverse effects in the physical makeup of the product.

So, when the cartons of clear plastic bottles or hip replacement surgical kits arrive at the radiation sterilizing facility, the manufacturer—after previous product testing—will specify that they are to receive a dose of, for example, between 25 and 40 kilogray (or maybe between 8 and 15 kGy, or 50 and 100 kGy). Paperwork containing information such as the number of pallets, pallet configuration, product dimensions, product density, and dose range, will begin to wind through various departments in the front office for various checks and approvals.

As noted earlier, the only variable involved with the actual gamma sterilization process is time—how quickly the product is shuttled past the source rack. Workers load the totes (the containers in which materials to be irradiated are placed) in accordance with orders received from the scheduling department, whose job of ensuring that those dose requirements are met requires, however, consideration of a whole host of interdependent variables. The scheduler must not only ensure that a dose requirement is met by determining a proper cycle time, but do so while maximizing efficiency and profitability of the cell, which is in operation for 24 hours a day, seven days a week.

Determining cycle time can be like opening one of those Russian nesting dolls that contain another doll to be opened up, and another, and so on. The scheduler must take into consideration the density of the package—higher density packages require slower cycle times. But this is affected not only by the individual components of the package, but also by how tightly packed they are. A box of heavy orthopedic implants may be less dense than a box of light surgical gloves because those gloves can be very tightly packed. And different manufacturers can pack their gloves at different densities.

The difference in cycle times due to density may be fourfold. "If I look at my entire product mix here," Valentyn said, "and I've got one box at the lightest, fastest cycle that I have, I could probably get it off . . . in about three hours. And on the [heavy] side, it could be 10 to 12."

While taking into consideration the density of the product to be processed, the scheduler must also determine how best to load the product into the totes to maximize the space, a basic commodity of the radiation contract sterilizer. "What we're selling is time and space," Meyer said. "[O]nce a tote is put on the system, we can't add anything to it. So, whether I have one box in a tote or a completely full tote, my costs are the same."

The dimensions of the tote resemble those of a shipping pallet. The aluminum tote is 40 in. high, and is framed by an opening that measures 48 in. wide by 24 in. deep. Some, but not all, manufacturers ship their product in boxes that match the "footprint" of the tote—so that they fit tightly but comfortably inside. Others will ship product in many smaller boxes, in which case the scheduler would need to figure out how best to position the boxes within the tote to maximize the space.

Last, the scheduler must also figure the best sequence in which to run the products. This can be a challenge, because no money is being made while the system is flushed between cycle groupings and empty totes are run through the cell (to ensure adjacent product runs receive the correct dose). "If I have all similar dose, I just keep adding and adding—it can go around forever," Meyer said. "However, if the customer has smaller volumes, especially if the dose and densities aren't the same as what I'm running, I have to break that cycle by adding empties because it's a different dose requirement. Therefore, I'm inefficiently putting buffer in."

Dose requirements, product density, carton size, the product mix at any given time—not to mention gradual compensations for source decay—are all elements the scheduler juggles in the calculation of cycle time. And that, according to Valentyn, is where the art of scheduling comes in.

Into the cell

At the heart of this SteriGenics facility is the Gemini gamma cell, in which two independent overhead conveyor lines bring product along either side of the Co-60 source rack. The greater flexibility and ability to turn around product quickly is obvious, as the two processing lines can allow heavy, dense prod-

Workers load totes with guidance from, left to right, a tote counter, a weigh scale, and a monitor that displays proper loading configurations.

uct to plod along on one side, and lighter, less dense product to speed through on the other.

Six-foot-thick concrete walls surround the cell, through which the carriers, hung under a conveyor system, travel along a symmetrical mazelike route. Three totes are stacked on each carrier: Each carrier contains three shelves, with room for one tote on each shelf. At any given time there are 12 carriers on each line moving through the system. The carriers wind through one labyrinthine side of the cell and cut across the longest straightaway as they slide alongside the approximately 19-ft-long source rack in the middle of the cell. The totes move broad-sided along the rack, and then wind back through a similar path on the other side of the cell. That's one run.

Because the source rack is raised at a level that is even with the middle tote of the carrier, the tote on the middle shelf receives the highest dose. To ensure an even distribution of dose, each tote will make a total of six trips past the gamma source. After a carrier's first pass, it's brought out, rotated 180° along its vertical axis, and run through again so the other side can be irradiated. After that second run, the tote on the first shelf is automatically moved up to the second, the tote on the second shelf is moved up to the third, and the tote on the third shelf is removed, and a new tote is positioned on the first shelf. The front and back of the tote carrier are then irradiated, and the totes are shuffled once again. Each tote always begins its processing run on the bottom shelf, and each tote always receives six exposures to the Co-60 source—two passes on each of the three shelves—ensuring a uniform dose distribution of each tote from side to side, top to bottom. The only human involvement during the entire process of the six passes is the initial loading and final unloading of totes; the tote shuffling is mechanized.

Dose verification

The process of verifying that the products have received a dose within the range of the manufacturer's requirements involves placing small, clear, plastic dosimeters in certain totes throughout the product run. When a product is sterilized for the first time at the facility, an extensive dose mapping procedure is performed to determine the dose distribution—the high and low dose positions—for that product. Once that is established, the maximum and minimum dose locations are monitored throughout the processing run to ensure that specifications are met. A likely routine dosimetry scheme would call for two dosimeters to be placed in the first and last totes of the product run, as well as in every 12th tote and after any breaks in the run that may occur for maintenance, troubleshooting, or other reasons. Location of the dosimeters within the tote will also vary from customer to customer because of different box configurations and weights.

When this facility opened in 1996, totes were loaded with dummy materials of different densities, such as foam, cardboard, and ceiling tiles, and run through the system to get an idea of dose mapping properties of different densities. "If your product comes to us [for the first time] and it is such-and-such a density and weight," Valentyn explained, "we have a pretty good idea of where [the dose mapping] would fall out based upon the commissioning data that was performed when we first opened the system."

Material considerations for radiation sterilization

Radiation's effects

Radiation interacts with polymers in two basic ways: chain scission, which results in reduced tensile strength and reduced elongation, and crosslinking, which results in increased tensile strength and reduced elongation.

Both reactions occur simultaneously. One, however, is usually predominant, depending upon the polymer and additives involved. Chain scission has been shown to affect stressed polymers (containing residual molding stress) more than other polymers. The combined effect of solvent-induced stress, residual molding stress, and applied load act to intensify radiation damage. This may account for the wide differences in radiation tolerance reported.

Generally, polymers that contain aromatic ring structures (e.g. polystyrene) are resistant to radiation effects, whereas the aliphatic polymers exhibit varying degrees of radiation resistance depending upon their levels of unsaturation and substitution.

The manufacturer's attention should focus on the possible effect of radiation on mechanical properties such as tensile strength, elastic modulus, impact strength, and elongation. Each may influence the device's performance and, therefore, should be evaluated by functional testing. Some effects of radiation, such as reduced elongation due to chain scission, may detract from the device's performance. In other cases, the effects of radiation can be beneficial. For example, crosslinking of polyethylene and silicones increases their tensile strength.

Radiation stabilizers and additives

Color change is another effect of radiation. While not related to changes in other physical properties, coloration may be relevant to market reaction to the product. Most polymer manufacturers have addressed this subject by using color-compensated materials or special additives, which minimize radiation-induced color changes.

Additives are usually included in small amounts (less than 1 percent) in commercial polymer products. Their primary purposes are to aid in processing, to stabilize the material, and to impart particular properties to the product.

Radiation stabilizers have been developed and are now available for many polymers. For example, tint-based, multi-function stabilizers are now commonly used to counteract PVC's (polyvinyl chloride) typical color change due to irradiation. Other additives, called antirads, which usually act as antioxidants, help prevent radiation damage.

These additives can act either as reactants, which readily combine with radiation-generated free radicals within the polymer, or as primary energy absorbers, preventing the interaction of the radiation energy with the polymer itself.

Material evaluation

When evaluating the radiation stability of a polymer and the ultimate success of a component or medical device, the following should be taken into consideration:

n Stabilizers and antioxidants added to a polymer can reduce the effects of irradiation on the device's mechanical properties and/or physical appearance;

■ Thin part sections, thin films, and fibers present in a component or device can allow for excessive oxygen exposure during the irradiation process, thus causing degradation of the polymer material;

■ Residual mold stress present after molding and assembly of a component or device can promote molecular scissioning during irradiation;

■ Highly oriented moldings which are strong in the axis of orientation but are already very weak in the cross-flow axis become weaker after irradiation; and

■ High molecular weight polymers having low melt flow will survive radiation better by providing longer molecules and stronger parts before and after irradiation.

Compatibility and validation

Each polymer reacts differently to ionizing radiation. Thus, it is important to verify that the maximum administered dose will not have a detrimental effect on the device's function or the patient's safety over the products' intended shelf life.

Experimental samples of the product should be irradiated to at least the highest dose to be encountered during routine processing. For example, a product which is to receive a sterilizing dosage of 25 to 40 kGy should be tested by dosing samples to at least 40 kGy. A conservative approach is to irradiate samples at doses up to twice the anticipated maximum dose.

Since various device applications call for certain performance properties or functional characteristics, it is important to test each device in an appropriate manner, using both new and aged product.—*SteriGenics International*

Because temperature and lighting can affect dosimetry readings, the dosimeters are analyzed using a spectrophotometer in an environmentally controlled room. The average of the two dosimeter readings, which are usually very close, is used to verify the dose. The dosimeters are retained for 30 days.

The dose data and other paperwork are then brought up to the front office for review. The quality assurance department reviews all the paperwork, investigates whether the dose requirements were met, and, if so, issues a certificate of irradiation. While the paperwork makes its final passes through the invoicing and customer support departments, the product itself is shrink-wrapped and is placed on the processed side of the warehouse, where it will await final release. That will complete a process that began four or five days previously when the product was dropped off, or about half the amount of time it would have taken if it were treated with EtO.

Safety measures

To an observer, the siren that *weeeooooos* through the warehouse when the source rack is lifted out of the shielding pool and into position is a visceral and unmistakable signal that something dangerous is occurring inside the cell. And that siren, as loud and stirring as it is, may as well be an afterthought given the number of redundant safety features that are already in place to protect against anyone's being anywhere near the source rack when it's out of the pool—anyone for whom the siren would actually matter.

To begin, there is a fence that prevents anyone from wandering into the cell randomly, and, when the system is shut down, the carriers are always positioned to block entrance to the cell. If someone were to climb the fence, pressure-sensitive mats on the other side would automatically drop the source rack into the shielding pool upon activation. Beyond the mats are photo-eyes that will shut the system down when movement is detected. To prevent anyone from being trapped in the cell during startup, the shift supervisor must walk through the entire system and insert a key—the only such key that exists—into several checkpoints throughout the cell, during which time he or she checks for anyone that may still be in the system. If someone were yet in the cell, there are various cables along the perimeter that can be pulled to immediately drop the source into the shielding pool. There is also a door leading out of the cell into the control room that is never locked, although it locks on the other side to prevent entry into the cell from the control room when the source is exposed. All these safety features meet requirements set by the Illinois Department of Nuclear Safety and the Nuclear Regulatory Commission.

Source maintenance

Managing the constantly decaying 4 000 000 curies of energy contained in the source rack's 550 or so Co-60 pencils, each with a half-life of 5.27 years and containing anywhere between 7000 and 11 000 curies, is not a task for the inexperienced. The pencils need to be swapped out or moved around periodically to ensure an even dose distribution throughout the rack, and the slowing of cycle times due to source decay will mandate the procedure. "At some point in time," Valentyn said, "you have to determine, Do I need to buy more isotope . . . [to] run faster, because my backlogs are starting to increase?"

A formidable amount of preparation will go into an isotope loading, which is usually performed once a year. "I have books that I could walk to," Valentyn explained, "and specifically tell you how many pencils we have, what the decay is today, what the decay is six months from now, and . . . based upon looking into the future, I can tell you where I'm going to be next June. Looking at customer demand, looking at volumes, looking at projections from sales forecasts, I can determine if I need to plan to do an isotope loading in six or nine months."

When performing a reloading, the facility will receive three or four shielded casks from the Co-60 pencil manufacturer, each cask holding a basket of approximately 20 Co-60 source pencils. The double-encapsulated stainless steel pencils measure 18 in. in length and 0.500–0.625 in. in diameter. Each pencil is loaded with a single row of Co-60 slugs and stamped with a serial number. Before the casks are delivered, the manufacturer will send a schematic illustrating how the pencils are arranged in the basket and how much energy each pencil contains. This allows the engineering group to prepare each step of the loading process. "So at the end, it's all been mathematically determined where you place these pencils to give you as much even, consistent distribution from one end of the source rack to the other," Valentyn said. The reloading will require the system to be shut down for 18 to 24 hours.

The job of getting the Co-60 pencils to their proper position essentially entails peering down into the approximately 20-ft-deep pool of water and manipulating the pencils using a

Top: The Gemini Cell has two conveyor lines, which cross here, that allow for simultaneous processing of disparate product. **Above:** The main activity area of the warehouse is the mezzanine, where workers load totes for processing and unload for shipment.

25-ft-long pole that has a hook on the end of it. There are special remote cameras and underwater lighting equipment to help with the task, but manual dexterity plays a large role in the loading. "We have our expertise and our SWAT team that we call," Valentyn said, "people that have been trained over the years . . . in manipulating these pencils.

"[We] can't do that for very long periods without taking a break. . . . We're at the water level, sitting on our knees next to the water, almost at the edge of the pool—wearing some knee pads because it's murder on your knees.

". . . But people typically enjoy—if they've never seen it—seeing a loading. We've got a few of our customers, our larger customers, that say, 'Hey, when you have a loading give me a call. I'd like to see how that takes place.'"

Saving time, making money

To a manufacturer, the more quickly a product can travel from the production plant to the customer, the better. The less time a carton of cleanroom towels spends between the manufacturing plant and a hospital is how much more quickly a manufacturer can invoice the customer—and how much more quickly money can be made. The amount of precise and perhaps tedious work that is done in the contract sterilizer's front office before the product is even loaded onto the conveyor is done so that the actual radiation sterilization procedure can unfold simply and quickly, and so appeal to profit-seeking manufacturers.

Load it, dose it, unload it, ship it NN