MEDICAL DEVICE REPORTING
FDA MEDICINE MANUFACTURERS

User Facility Reporting

Issue No. 39 *A quarterly bulletin to assist hospitals, nursing homes, and other device user facilities* Summer 2002

AUGUST 14: IMPORTANT ENFORCEMENT DATE FOR REPROCESSING OF SINGLE-USE DEVICES

On August 14, 2002, hospitals that reprocess single-use devices (SUDs) must meet all of the regulatory requirements of a device manufacturer under the Federal Food, Drug, and Cosmetic Act as amended. These requirements include:

- Establishment registration and device listing
- Premarket clearance or approval
- Labeling
- Corrections and removals
- Medical device tracking
- Medical device reporting (MDR)
- Quality system regulation (QS).

For additional information about SUDs reprocessing, visit the Reuse Website at: http://www.fda.gov/cdrh/reuse/index.shtml. The following tables summarize the regulatory requirements that hospital reprocessors of SUDs must meet.

DATES FOR MEETING PREMARKET SUBMISSION REQUIREMENTS

PMA Applications (Premarket Approval) or 510(k) Submissions (Premarket Notification)	Due by:	Cleared or approved by:
Class III	February 14, 2001	February 14, 2002
Class II non-exempt	August 14, 2001	August 14, 2002*
Class I non-exempt	February 14, 2002	August 14, 2002

*Provided that the reprocessor
(1) submitted a premarket notification by August 14, 2001;
(2) has not received a "not substantially equivalent" determination; and
(3) provides timely responses to the Food and Drug Administration's requests for additional information.

DATES FOR MEETING NON-PREMARKET REQUIREMENTS

Registration and Listing	August 14, 2001
Medical Device Reporting (MDR)	August 14, 2002
Tracking	August 14, 2002
Corrections and Removals	August 14, 2002
Quality System Regulation	August 14, 2002
Labeling	August 14, 2002

In This Issue:

CELL PHONES IN HEALTHCARE FACILITIES: USE WITH CAUTION*

By Julia Marders, RN, MS, and Donald Witters, MS

A patient in the intensive care unit was receiving epinephrine by an infusion pump when a visitor received a cell phone call. When the phone was answered, the infusion pump increased the rate of the drip. The patient received an unintended bolus of medication and subsequently developed epinephrine toxicity.

What went wrong?

Under certain conditions, cell phone radio transmissions can cause electromagnetic interference (EMI) and disrupt the functioning of electrically powered medical devices as in this case with an infusion pump. EMI related patient injuries are relatively rare, but sources of electromagnetic energy such as radio signals, AC power line disruptions, and electrostatic discharge can disrupt medical device performance. Most medical devices are tested for EMI and meet applicable performance standards, but in certain situations medical devices may be susceptible to potentially serious problems.

What precautions can you take?

- Educate yourself and your colleagues about the potential for EMI with medical devices and learn how to recognize and report problems.
- Develop and follow policies and procedures to ensure electromagnetic compatibility, especially in areas where critical-care devices are used. For more information, refer to the Food and Drug Administration's Web site at http://www.fda.gov/cdrh/emc/index.html.
- Manage the use of radio transmitters near electrically powered medical devices. Post signs prohibiting cell phone use where necessary. Make sure all patients, visitors, and staff members understand and adhere to these policies.
- If a death, serious injury, or device malfunction occurs because of actual or suspected EMI, notify the person in your facility responsible for reporting adverse events to the manufacturer and/or the Food and Drug Administration. You may voluntarily report a medical device problem by calling FDA's MedWatch reporting system at 1-800-FDA-1088; by fax: 1-800-FDA-0178); or on-line at http://www.fda.gov/medwatch.

Julia Marders is a nurse-consultant in the Center's Office of Surveillance and Biometrics, and Donald Witters is a biomedical engineer in the Office of Science and Technology and Chairman of the Electromagnetic Compatibility Group in the Center.

*Based on the authors' article "Don't Answer That Cell Phone" that was published in the June issue of *Nursing 2002*.

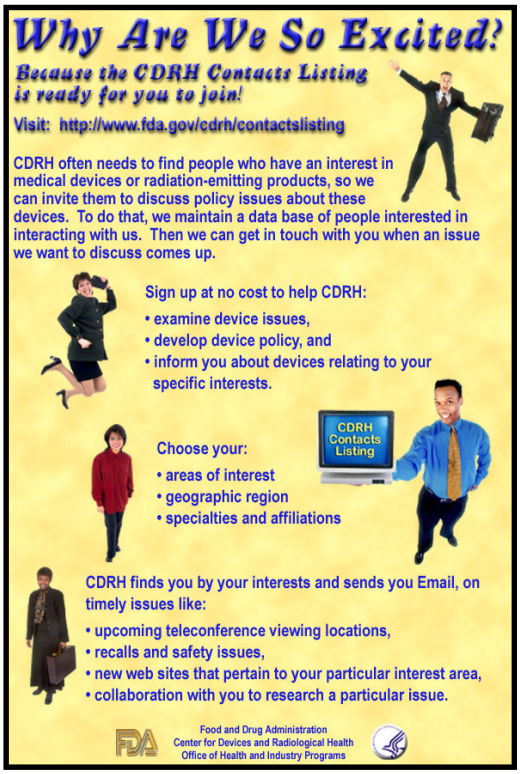
REUSE CD ROM AVAILABLE

The Center for Devices and Radiological Health developed a CD ROM entitled: **"An Overview of the Regulatory Requirements for Reprocessing of Single-Use Devices by Hospitals."** While supplies last, a free copy of the CD-ROM is available by request at http://www.fda.gov/cdrh/reuse/reuse-important.shtml.

The two-disc set covers the regulatory requirements that a hospital must meet if it reprocesses single-use devices (SUDs). Topics include:

- Introduction about reprocessing SUDs
- Premarket Review
- Corrections and Removals
- Problems with Reprocessing
- Quality System Regulation
- Registration and Listing
- Labeling
- Medical Device Tracking
- Medical Device Reporting
- Useful Information

To see the PowerPoint presentations from the CD ROM, visit the Reuse Events Page at http://www.fda.gov/cdrh/reuse/reuse-events.shtml.



LATEX ALLERGY: RECENT DEVELOPMENTS IN GLOVE USE AND SAFETY

By Vesna J. Tomazic-Jezic, Ph.D.

In the 10 years since allergy to natural rubber latex (NRL) was identified as a serious concern for frequent users of medical gloves, researchers have worked to minimize or prevent allergic reactions and future sensitization.

The use of medical gloves has continued to increase (at an annual rate of 2.6 percent) because of the need for reliable protection from blood-borne pathogens. This trend will probably continue at a similar pace. However, the recent threat of possible bioterrorism acts will probably increase the use of protective gloves.

The notable progress in managing latex allergy was achieved by: (1) reducing the potential of NRL gloves to cause allergic reactions and (2) developing better diagnostic tests to evaluate product allergenicity.

Today's gloves have less potential for sensitization than gloves of a decade ago. As a result of intensive research, increased regulatory controls, and educational activities, manufacturers have improved their products. The table below shows a general trend in glove use and a rough estimate of protein and powder level changes between 1990 and 2002. In parallel to the advances in technology of glove production, there has been significant progress in the diagnostic methodology and assays for evaluation of product allergenicity. The American Society of Testing and Materials (ASTM) developed new standard methods for antigenic proteins (D6499) and glove powder measurement (D6124). The ASTM also determined standard maximum limits for protein and powder levels that are included in pre-existing glove standards D3577 and D3578.

"As a result of intensive research, increased regulatory controls, and educational activities, manufacturers have improved their products."

	1990-1992	2000-2002
Total glove use in USA	3-5 billions	28-30 billions
Protein levels	Up to 5000 µg	Up to 1800 µg
Powder levels	Up to 500 mg	Up to 100 mg

With the widespread usage of natural latex gloves, the problem f allergy to NRL proteins is still an important issue. Better choices of less allergenic gloves and implementation of other preventive measures should reduce the extent and the intensity of the problem. Recent epidemiological studies indicate that the average prevalence of sensitivity in occupationally latex-exposed individuals is lower than reported several years ago. Similarly, the incidence of adverse reactions decreased as sensitized individuals are better informed and have better products. The progress is encouraging, but efforts must continue until the problem of latex allergy is resolved. The Food and Drug Administration is presently preparing a new regulation that would further improve the safety of NRL gloves.

Dr. Vesna J. Tomazic-Jezic is a research biologist in the Center's Office of Science and Technology.

ELECTRONIC NOTIFICATION FOR THE *USER FACILITY REPORTING BULLETIN* IS NOW AVAILABLE

If you would like to be notified electronically (via e-mail) when a new issue of the *User Facility Reporting Bulletin* is released, you can sign-up for our List Service at:

http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCDRHNew/listman.cfm

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
9200 Corporate Boulevard
Rockville, MD 20850

July 12, 2002

Public Health Notification: PVC Devices Containing the Plasticizer DEHP

(You are encouraged to copy and distribute this information)

Dear Colleague:

This is to inform you that FDA's Center for Devices and Radiological Health completed its safety assessment of Di(2-ethylhexyl)phthalate (DEHP) released from polyvinyl chloride (PVC) medical devices in September, 2001, and to advise you of steps that you can take to reduce the risk of exposure in certain populations.

Devices Affected

PVC is a plastic polymer that is used in a wide array of products. Unplasticized PVC is hard and brittle at room temperature. A plasticizer (softener) is typically added to increase the flexibility of the polymer. DEHP is the plasticizer for most PVC medical devices.

Devices that may contain DEHP-plasticized PVC include:

- intravenous (IV) bags and tubing
- umbilical artery catheters
- blood bags and infusion tubing
- enteral nutrition feeding bags
- nasogastric tubes
- peritoneal dialysis bags and tubing
- tubing used in cardiopulmonary bypass (CPB) procedures
- tubing used in extracorporeal membrane oxygenation (ECMO)
- tubing used during hemodialysis

Nature of the Problem

Everyone is exposed to small levels of DEHP in everyday life. However, some individuals can be exposed to high levels of DEHP through certain medical procedures. DEHP can leach out of plastic medical devices into solutions that come in contact with the plastic. The amount of DEHP that will leach out depends on the temperature, the lipid content of the liquid, and the duration of contact with the plastic. Seriously ill individuals often require more than one of these procedures, thus exposing them to even higher levels of DEHP.

Exposure to DEHP has produced a range of adverse effects in laboratory animals, but of greatest concern are effects on the development of the male reproductive system and production of normal sperm in young animals. We have not received reports of these adverse events in humans, but there have been no studies to rule them out. However, in view of the available animal data, precautions should be taken to limit the exposure of the developing male to DEHP.

Risk determinants

Two factors determine the degree of risk posed by exposure to DEHP in a medical setting. The first is the patient's sensitivity to DEHP. Based on the evidence cited above, the male fetus, male neonate, and peripubertal male would appear to be high-risk groups. The second factor is the dose of DEHP received by the patient. This is determined largely by the type of procedure performed, as well as the frequency and duration of these procedures.

PUBLIC HEALTH NOTIFICATION - *Continued*

Highest risk procedures

We examined the potential risk of exposure posed to patients by comparing the dose of DEHP that patients might receive during various procedures to a "Tolerable Intake" (TI) value for the compound.

The following procedures have been identified as posing the highest risk of exposure to DEHP:

- exchange transfusion in neonates
- ECMO in neonates
- total Parenteral Nutrition (TPN) in neonates (with lipids in PVC bag)
- multiple procedures in sick neonates (high cumulative exposure)
- hemodialysis in peripubertal males
- hemodialysis in pregnant or lactating women
- enteral nutrition in neonates and adults
- heart transplantation or coronary artery bypass graft surgery (aggregate dose)
- massive infusion of blood into trauma patient
- transfusion in adults undergoing ECMO

In contrast, there is little or no risk posed by patient exposure to the amount of DEHP released from PVC IV bags during the infusion of crystalloid fluids (e.g., normal saline, D5W, Ringer's Lactate). Further, there is little risk posed by exposure to the amount of DEHP released from PVC bags used to store and administer drugs that require a pharmaceutical vehicle for solubilization, when label instructions are followed.

Recommendations

Most importantly, you should not avoid the procedures cited above simply because of the possibility of health risks associated with DEHP exposure. The risk of not doing a needed procedure is far greater than the risk associated with exposure to DEHP.

For some of the above procedures, PVC devices that do not contain DEHP can be substituted, or devices made of other materials (such as ethylene vinyl acetate (EVA), silicone, polyethylene or polyurethane) can be used, if available. If PVC devices containing DEHP must be used, you may be able to minimize exposure to DEHP by, for example, using the freshest possible blood products stored at the lowest possible temperature, or by using heparin-coated ECMO circuits.

We recommend considering such alternatives when these high-risk procedures are to be performed on male neonates, pregnant women who are carrying male fetuses, and peripubertal males. One source for identifying alternative devices that do not contain DEHP-plasticized PVC is http://www.sustainablehospitals.org, associated with the University of Massachusetts Lowell.

For other patient groups, who are presumably at lower risk, the decision to use DEHP alternatives must take into account the medical advantages and drawbacks of the substitute materials and their availability.

Reporting Adverse Events to FDA

The Safe Medical Devices Act of 1990 (SMDA) requires hospitals and other user facilities to report deaths and serious injuries associated with the use of medical devices, including the devices cited above. We request that you follow the procedures established by your facility for such mandatory reporting.

We also encourage you to report other adverse events associated with the use of medical devices. You can report these directly to the device manufacturer. You can also report to MedWatch, the FDA's voluntary reporting program. You may submit reports to MedWatch one of four ways: online at http://www.accessdata.fda.gov/scripts/medwatch, by telephone at 1-800-FDA-1088; by FAX at 1-800-FDA-1078; or by mail to MedWatch, Food and Drug Administration, HF-2, 5600 Fishers Lane, Rockville, Maryland 20857.

PUBLIC HEALTH NOTIFICATION - *Continued*

Getting More Information

The complete safety assessment, "Safety Assessment of Di(2-ethylhexyl)phthalate (DEHP) Released from PVC Medical Devices," can be found on the CDRH web site at http://www.fda.gov/cdrh/ost/dehp-pvc.pdf. Should you have questions concerning this letter, please contact Laura Alonge, Office of Surveillance and Biometrics (HFZ-510), 1350 Piccard Drive, Rockville, Maryland 20850, by fax at 301-594-2968, or by e-mail at phann@cdrh.fda.gov. Additionally, a voice-mail message may be left at 301-594-0650 and your call will be returned as soon as possible.

All of the FDA medical device postmarket safety notifications can be found on the World Wide Web at http://www.fda.gov/cdrh/safety.html. Postmarket safety notifications can also be obtained through e-mail on the day they are released by subscribing to our list server. You may subscribe at http://list.nih.gov/archives/dev-alert.html.

Sincerely yours,

/s/

David W. Feigal, Jr., M.D., M.P.H.
Director,
Center for Devices and Radiological Health

FDA Public Health Web Notification: Cochlear Implant Recipients may be at Greater Risk for Meningitis

July 24, 2002

Updated: August 15, 2002

(You are Encouraged to Copy and Distribute this Notification)

The FDA has become aware of a possible association between cochlear implants and the occurrence of bacterial meningitis. The cause of meningitis in these cochlear implant recipients has not been established. The design of the electrode is being considered as a possible factor.

Over a period of 14 years, 52 cases of meningitis have been reported worldwide to Advanced Bionics Corporation and Cochlear Corporation. These have occurred in children and adults ranging in age from 21 months to 72 years who have undergone cochlear implantation for severe to profound deafness. A total of 12 known deaths have resulted from these cases. Two implant surgeons, Drs. Noel Cohen and Thomas Balkany, have recently surveyed cochlear implant centers and manufacturers in North America. They identified 22 cases (of the 52 worldwide cases) of meningitis. Nine cases were identified in patients with the Advanced Bionics CLARION device, 13 cases with the Cochlear Nucleus device, and no cases with the MED-EL Corporation device.

Cerebrospinal fluid culture results are available in 14 cases. Although most cases have been caused by *Streptococcus pneumoniae* (pneumococcus), other organisms -- including *Hemopohilus influenza*, enterococcus, *E. coli*, and *S. viridans* -- have been cultured. The vaccination history against pneumococcus was available in 6 cases and none had been vaccinated. The onset of meningitis symptoms ranged from less than 24 hours to greater than 5 years from

PUBLIC HEALTH WEB NOTIFICATION - *Continued*

time of implant. Most of the patients have been children, predominantly under the age of 5, but some adults with cochlear implants have also developed meningitis.

The cause of meningitis in these cochlear implant recipients has not been established. Some deaf patients may have congenital abnormalities of the cochlea (inner ear) which predispose them to meningitis even prior to implantation. Patients who become deaf as a result of meningitis are also at increased risk of subsequent episodes of meningitis compared to the general population. Other predisposing factors may include young age (< 5 years), otitis media, immunodeficiency, or surgical technique. The cochlear implant, because it is a foreign body, may act as a nidus for infection when patients have bacterial illnesses.

Design of the electrode is also being considered as a possible predisposing factor. The Advanced Bionics CLARION device differs from other currently marketed cochlear implants because it uses an additional piece (i.e., a positioner) which is introduced next to the electrode into the cochlea to facilitate transmission of sound information to the auditory nerve. During an ad hoc meeting in Amsterdam on July 5, 2002, a group of European physicians concluded that there were more cases of meningitis with the CLARION device than with other cochlear implants and that this difference may be attributable to the use of the positioner. The organizers of this meeting recommended that the use of the positioner be discontinued, and the regulatory authorities of several European countries (e.g., France, Germany, and Spain) have accepted these recommendations. Consequently, Advanced Bionics has agreed to discontinue use of the positioner in these countries and will be marketing one of their current electrode systems (HiFocus) without the positioner. The company has also initiated a voluntary recall of any unimplanted CLARION devices in the United States and has announced that it will be seeking FDA approval for the HiFocus electrode without the positioner.

Cochlear Corporation, in reviewing all data from North American patients implanted with the Nucleus device, claims to have an overall incidence of reported meningitis that is comparable to the incidence of meningitis in the general population. Cochlear Corporation noted that the majority of the reported cases of meningitis in these implanted patients had predisposing factors for meningitis (e.g., Mondini deformity, prior history of meningitis).

Meningitis

Meningitis is an infection of the lining of the surface of the brain. Early symptoms of meningitis include fever, irritability, lethargy, and loss of appetite in infants and young children. Older children and adults may also manifest headache, stiff neck, nausea and vomiting, and confusion or alteration in consciousness. Physicians are encouraged to consider a diagnosis of meningitis in cochlear implant patients when such symptoms exist and to begin appropriate diagnosis and treatment as soon as possible.

The younger patient population (< 5 yr) and the elderly are most vulnerable to meningitis.

Cochlear Implants and Otitis Media

In some of the reported cases of meningitis in cochlear implant recipients, patients may have had overt or sub-clinical otitis media prior to surgery or before the meningitis developed. Physicians are encouraged to consider appropriate prophylactic perioperative antibiotic treatment, and to diagnose and treat otitis media promptly in patients with cochlear implants.

Cochlear Implants and Vaccination

Cochlear implant candidates, as well as those already implanted, may benefit from vaccinations against organisms that commonly cause bacterial meningitis, particularly *Streptococcus pneumoniae* and *Haemophilus influenzae*. The immunization status should be ascertained for all candidates for cochlear implants prior to surgery as well as for those with an existing implant. Cochlear implant patients should consult their physicians about receiving immunizations.

PUBLIC HEALTH WEB NOTIFICATION - *Continued*

At least one cochlear implant manufacturer provides reimbursement for vaccination.

- *Haemophilus influenzae* conjugate vaccines are recommended by the Advisory Committee on Immunization Practices (ACIP) for all children up to age 5 years.
- Heptavalent pneumococcal conjugate vaccine (Prevnar®) is indicated for use in infants and toddlers, and is recommended by the ACIP for all children less than age 2 years, and for children up to age 5 years who are at high risk of invasive pneumococcal infections.
- The 23-valent pneumococcal polysaccharide vaccines (Pnu-Imune®23 and Pneumovax®23) are recommended for children over age 2 years, adolescents, and adults who are at high risk of invasive pneumococcal disease.
- For children age 2 years to 5 years of age who are at high risk of invasive pneumococcal infections, ACIP recommends use of pneumococcal conjugate vaccine followed at least 2 months later by 23-valent pneumococcal polysaccharide vaccine, in order to provide protection against a broader range of serotypes, although supporting data are limited[1]. See individual product labeling for information on dosing and scheduling of the vaccines.

For additional information regarding immunizations refer to the National Vaccine Program Office of the Centers for Disease Control and Prevention (http://www.cdc.gov/od/nvpo/).

Reporting Cases of Meningitis in Cochlear Implant Recipients

We encourage you to report cases of meningitis in cochlear implant recipients. You can report these directly to the device manufacturer or you can report them to MedWatch, the FDA's voluntary reporting program. You may submit reports to MedWatch one of four ways: online at http://www.accessdata.fda.gov/scripts/medwatch/ by telephone at 1-800-FDA-1088; by FAX at 1-800-FDA-0178; or by mail to MedWatch, Food and Drug Administration, HF-2, 5600 Fishers Lane, Rockville, MD 20857.

FDA Contact

Nancy Pressly
Office of Surveillance and Biometrics (HFZ-510)
1350 Piccard Drive, Rockville, Maryland, 20850
Fax at 301-594-2968, or by e-mail at phann@cdrh.fda.gov

Additionally, a voice mail message may be left at 301-594-0650 and your call will be returned as soon as possible.

[1]Preventing Pneumococcal Disease Among Infants and Young Children Recommendations of the Advisory Committee on Immunization Practices (ACIP) October 06, 2000 / 49(RR09);1-38.

USER FACILITY REPORTING BULLETIN

FDA produces the *User Facility Reporting Bulletin* quarterly to assist hospitals, nursing homes, and other medical device user facilities in complying with their statutory reporting requirements under the Safe Medical Devices Act of 1990, the Medical Device Amendments of 1992, and the Food and Drug Administration Modernization Act of 1997. The *Bulletin's* contents may be freely reproduced. Comments should be sent to the Editor.

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