



# HIPEC

## Legal and Environmental Aspects



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# **Legal considerations and HIPEC**

**(in most countries)**

## **Labour Code defines Obligations for the head of establishment**

- 1. Risk assessment**
  - 2. General and specific preventive measures for carcinogenic, mutagenic and toxic agents**
  - 3. Criminal law applicable to a head of establishment who infringes any of these provisions**
- 1. Entitlement to alerting and withdrawing personnel**

# A Challenge

## Mixing chemotherapy and hyperthermia with surgery

- **Major Surgery**
- **HIPEC combines the therapeutic effects**
  - **Cytotoxic drugs**
  - **Heating procedure (medical device)**
- **Secondary effects of chemotherapy**
- **Safe conditions for the patient and the staff must be preserved**

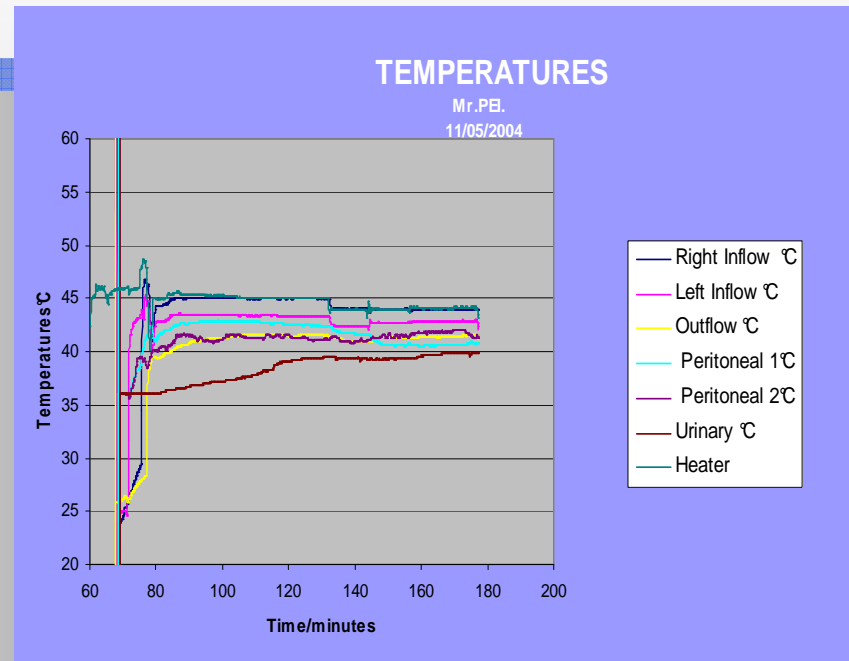
# The risk of Surgery

- **Complete cytoreductive surgery**
- **Major abdomino-pelvic surgery**
  - Long lasting: 3 to 10 hours
  - Surgical resection of the primary tumor
  - several bowel resections
  - involved peritoneum exeresis
    - visceral and parietal peritonectomies
    - Glisson capsula
    - Diaphragmatic cupola
- **Morbidity-Mortality of such surgery**
- **Risk-Benefit analysis for each patient**

# The risk of hyperthermia

## Safety Instruction

- Patient's temperature  $\leq 39$  degreesC (102.2degreesF)
- Precisely Monitored and recorded Temperature
  - Oesophageal and bladder probes
  - Circuit Inflow and Outflow probes
  - Peritoneal probes
- Cooling blanket
- Risk of heat stroke syndrom



# Heat Stroke syndrom

- **During the heating time of HIPEC**
- **If the patient is not cooled down**
- **Symptoms of heat stroke syndrome**
  - **Increased core temperature  $\geq 39^{\circ}\text{C}$**
  - **Increased sweating**
  - **Hemodynamic disturbances**
    - **hypotension,**
    - **peripheral vasodilation, and**
    - **tachycardia**
  - **decreased urinary out-put**
- **Treatment : additional cooling**

# **The risk of Chemotherapy**

## **Evolution of Guidelines on Hazardous Drugs**

- **American Society of Health-System Pharmacists**
  - 1985, 1990
  - 2005: Guidelines on Handling Hazardous Drugs
- **NIOSH (Nat. Institutes of Occupational Safety & Health)**
  - 2004: NIOSH Hazardous Drug Alert
- **OSHA (Occupational Safety & Health Administration)**
  - 1986
  - 1995: Controlling Occupational Exposure to Hazardous Drugs

# **Workers potentially exposed hazardous drugs during HIPEC**

- **Operating room personnel**
- **Physicians, anaesthesiologists, surgeons**

**But also**

- **Shipping and receiving personnel**
- **Pharmacists and pharmacy technicians**
- **Nursing personnel**
- **Environmental services personnel**
- **Laboratory personnel**

# **Workplace exposure has been shown to induce**

- **health effects such**
  - **skin rashes,**
  - **decreased fertility**
  - **spontaneous abortions**
  - **congenital malformations**
  - **leukemia and other cancers**

# The risk of chemotherapy for surgeon and personnel

- preparation
- administration,
- waste disposal
- transport of cytotoxic agents
  
- Occupational hazards arise from
  - aerosolization
  - contacts including projections of cytotoxic agents

# Alternative Duty for

- **Pregnancy**
- **Breast-feeding**
- **Attempting to conceive or father a child**
- **Medical and exposure history**
  - Assessment and documentation of symptom complaints
  - Physical findings and laboratory values
- **immunocompromised**

# OSHA

## Occupational Safety & Health Administration

### U.S. Department of Labor

- **Guidelines for antineoplastic drugs in 1986**
- *OSHA Technical Manual*
- **Main elements of these 1999 OSHA guidelines include the following**
  - **Categorization of drugs as hazardous**
  - **Hazardous drugs as occupational risks**
  - **Work area**
  - **Prevention of employee exposure**
  - **Medical surveillance**
  - **Hazard communication**
  
  - **Training and information dissemination**
  
  - **Record keeping**

## Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings

- **NIOSH Publication No. 2004-165**

- POTENTIAL FOR WORKER EXPOSURE

- CONDITIONS FOR EXPOSURE

*Performing certain specialized procedures (such as intraoperative intraperitoneal chemotherapy) in the operating room [White et al. 1996; Stuart et al. 2002]*

- EXPOSURE ROUTES

- inhalation, skin contact

- EVIDENCE FOR WORKER EXPOSURE

- Drug handling circumstances (preparation, administration, or disposal)

- Amount of drug prepared

- Frequency and duration of drug handling

- PPE

- EVIDENCE FOR HEALTH EFFECTS IN WORKERS

- Mutagenicity

- Developmental and Reproductive Effects

- Cancer

## **Personal Protective Equipment for Health Care Workers Who Work with Hazardous Drugs**

- **Gloves**
- **Gowns**
- **Respiratory Protection**
  - NIOSH-certified N-95 (no protection against gases and vapors and little protection against direct liquid splashes)
  - full-facepiece chemical cartridge-type respirator [42 CFR 84; NIOSH 2005]
- **Eye and Face Protection**
  - face shields in combination with goggles
  - Do not use eye glasses or safety glasses with side shields
- **Sleeve, Hair, and Shoe Covers**
- **PPE Disposal**
  - Consider all PPE worn when handling hazardous drugs as being contaminated

# Controls

- **Staff orientation, training, education, and competency assessment**
- **Training programs to reduce worker risk**
- **Identifying indicators of exposure or early disease**
- **Medical monitoring program**
- **Requirements for Prescribing Chemotherapy**
- **Requirements for Preparation**
- **Basic Requisites for Order Processing and Checking of Chemotherapy**

# Requirements for Prescription

- **Chemotherapy orders must be written on**
  - Physician Order Form (or)
  - Medical staff approved Chemotherapy Order Form
- **Basic requisites for prescribing chemotherapy**
  - Drug name**
    - Complete, approved generic drug names (abbreviations should be avoided).
    - Only specific drug names that have been officially approved by the medical staff are acceptable.
  - Dosage**
    - Expressed in dose per body weight or body surface area
    - Total dose. For example, Cisplatin 80 mg/m<sup>2</sup>=128 mg
    - Diluent name and volume

# Requirements for Preparation

- **Strict control of the pharmacist**
- **Preparation sheets and prescription book**
- **Centralised preparation unit**
  - **Class II or III biological safety cabinets (BSC)**
  - **preparation hood**, with an aspirating vertical flow
  - **sterile clothing (overall, gloves, boots, mask, bonnet)**
- **Transport in a plastic bag or specific container**

# Requirements for Administration

- **Personal protective equipment (PPE)**
  - Long-sleeved disposable, low permeability gown , with knit cuffs
  - Unpowdered surgical gloves
  - Safety glasses
  - Special mask respirators
- **Avoid Chemotherapy aerosolization**
- **Spill procedures (Spill kit available)**
- **Cytotoxic waste clean up**
  - BIOHAZARD labeled, puncture-resistant waste container**for Contaminated needles and sharps**
  - BIOHAZARD labeled waste container

# Disposable Personal Protective Equipment (PPE)



- Double pair of gloves (nitrile ou vinyl) changed every 30 minutes,
- Special gown
- NIOSH-certified N-95 mask changed every 2 hours
- Safety glasses
- Charlotte



# Disposable Personal Protective Equipment (PPE)



Chemotherapy gloves



air-purifying mask respirators



Safety glasses



# Spill procedures

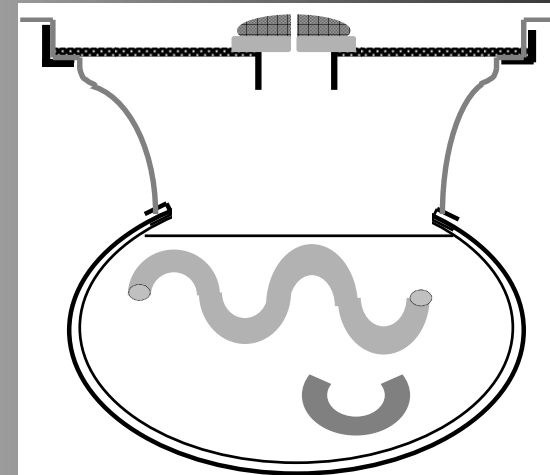
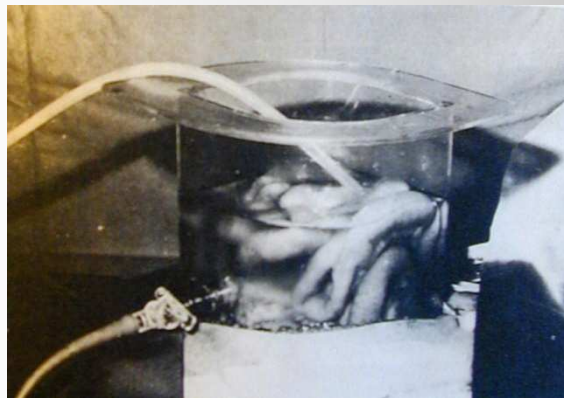
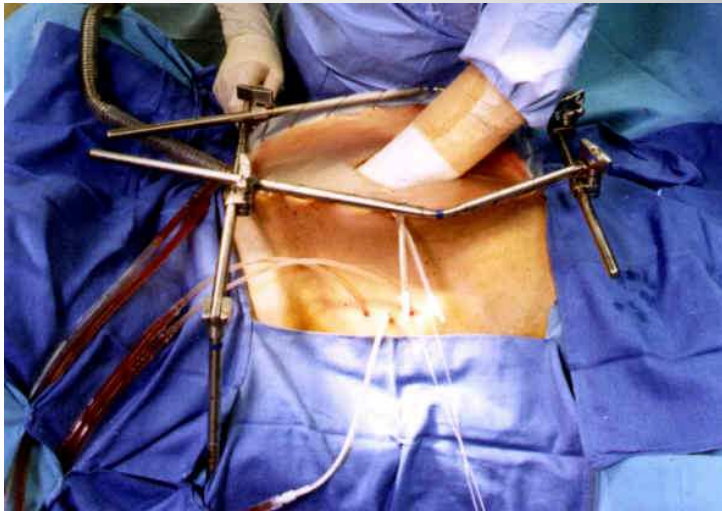
## spill kit contains the following items

- Impervious gown, safety shield, Green Z solidifier
- 1 pair extra strength latex gloves
- 1 pair vinyl gloves
- Pick-up scoop and scrapper
- 2 wiper pads
- 12" x 12" Barrier Super Zorb sheet
- Container for sharps disposal
- Identification tag
- Instructions
- Poly - bagged



# To avoid aerolization

## Opened system



# To avoid aerolization

## Closed system



# Cytotoxic waste clean up

- Fluid , Tubing
  - Contaminated PPE
- are placed in yellow BIOHAZARD labeled waste container



- Syringes, sharps
- are placed in BIOHAZARD labeled puncture-resistant waste container



**All containers are to be removed at the conclusion of the procedure**

# Measures after accidental contact with cytotoxic agents

- **Eye Contact**
  - Flush the affected eye(s) of clean water or normal saline
  - minimum 15 minutes
- **Skin Contact**
  - Remove any contaminated clothing
  - Wash the affected area with soap and water
  - minimum of 15 minutes
- **Skin Punctures**
  - Wash the puncture site thoroughly with soap and running water
  - 15 minutes.
  - Allow wound to bleed freely
  - Refer to extravasation policy
- **Obtain medical attention**
- **Document exposure in employee's medical record and medical surveillance log**

# Medical Device (FDA definition)

**An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, that is:**

- **Recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them**
- **Intended for use in the diagnosis of diseases or other conditions, or in the cure, mitigation, treatment, or prevention of disease in man or other animals; or**
- **Intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its principal intended purposes.**

# Medical Device (MDD definition)

The European Council Directive 93/42/EEC of 14 June 1993,  
concerning medical devices

- **Any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the manufacturer to be used for human beings for the purpose of:**
  - **Diagnosis, prevention, monitoring, treatment or alleviation of disease;**
  - **Diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap; Investigation, replacement or modification of the anatomy or of a physiological process;**
  - **Control of conception;**
  - **Which does not achieve its principle intended action in or on the human body by pharmacological; immunological or metabolic means, but which may be assisted in its function by such means.**

# **Medical Device** (*Canadian Food & Drugs Act* and the CMDRs definition)

- **An article, instrument, apparatus or contrivance, including a component, part or accessory of one, that is manufactured, sold or represented for use in:**
  - The diagnosis, treatment, mitigation or prevention of a disease, disorder or abnormal physical state, or its symptoms, in a human being;
  - The restoration, correction or modification of a body function or the body structure of a human being;
  - The diagnosis of pregnancy in a human being; or
  - The care of a human being during pregnancy and at and after the birth of a child, including the care of the child.
  - It includes a contraceptive device but does not include a drug

# Competent Authorities for Medical Device Regulation

- **FDA** **The US Food and Drug Administration:** the authority that regulates the manufacture of food, drugs, biologics and devices in the US.
  - *Safe Medical Devices Act*  
(A US law, enacted in 1990, which broadens the FDA's authority to regulate medical devices)
- **Health Canada** The organization that regulates medical devices in Canada, under the authority of the *Canadian Food and Drugs Act*.
  - Canadian Medical Devices Regulations (CMDRs)
- **Medicines and Healthcare products Regulatory Agency (MHRA)**  
The UK Competent Authority for the MDD
- **MDD (Medical Device Directive)**  
The European Council Directive 93/42/EEC of 14 June 1993, concerning medical devices.

# The European Union Requirements

- **PD ISO/TR 14969: 2004 Medical devices**  
International Organization for Standardization  
models for quality assurance
- **CE Marking**
  - The CE marking must be applied to all medical devices sold within the EU to demonstrate that the device conforms to the essential requirements of the MDD

# CE Marking

- **The mark that may be applied to a product to demonstrate that it conforms to the requirements of a European Directive**
- **The CE marking must be applied to all medical devices sold within the EU to demonstrate that the device conforms to the essential requirements of the MDD**

# **Key Elements of the MDD (medical device directive)**

- **Essential Requirements :**
  - patient safety, product performance, safety in use**
  - transportation and storage risks and benefits**
  - design and construction requirements**
- **Product Class**
- **Conformity Assessment Routes**
- **Technical Documentation**
- **Declaration of Conformity**
- **Postmarket Surveillance**
- **Vigilance Reporting**
- **European Authorized Representative**

# Six Steps to Acquiring the CE Marking

- **Classify Your Product** four classes (I, IIa, IIb and III)
- **Select the Best Conformity Assessment Route**
- **Apply for Registration**
  - **Selecting a Notified Body**
  - **The Process** (information, audit, examination)
  - **Registration Cost**
- **Provide Technical Documentation**
- **Make Declaration of Conformity**
- **Affix the CE Marking**

# Other Features of the CE Marking Process

- **Postmarket Surveillance and Vigilance Reporting**
- **European Authorized Representative**
- **Labelling**
  - **European Medical Device Labeling**
  - **Language Requirements**

# Vigilance Reporting

- **A requirement under the MDD, whereby member states must ensure that any reports of adverse incidents involving medical devices in the marketplace are recorded and evaluated centrally**
- **Manufacturers must put in place procedures to respond to such reports, by evaluating the causes, reporting findings to competent authorities and taking the necessary corrective action**

# HIPEC

## Medical Devices available in France

<b>Dispositif</b>	<b>Fabricant/ distributeur</b>	<b>Marquage CE</b>	<b>Autorisation FDA</b>
<b>Cavitherm</b>	<b>EFS (France)</b>	<b>Novembre 2005</b>	<b>Non</b>
<b>SunChip</b>	<b>Gamida tech France</b>	<b>Janvier 2006</b>	<b>Non</b>
<b>Performer LRT</b>	<b>Rand(Italie)/ medtronic</b>	<b>Janvier 2006</b>	<b>Non</b>
<b>ThermoChem HT-1000</b>	<b>ViaCirqu- thermaSolutionUS A/IST cardiology(France</b>	<b>Novembre 2005</b>	<b>Non</b>

# EC-CERTIFICATE

**CAVITHERM® made by EFS Electronique has been approved for the EC mark since January 2005 as a class IIb medical device (notified body: GMED).**

		<b>ATTESTATION/ CERTIFICATE N° 0430 / B3 / 4</b>			
Certification Médical-Santé		Délivrée à Paris le 1 <sup>er</sup> janvier 2005 Issued in Paris on January 1 <sup>st</sup> , 2005			
<b>ATTESTATION CE / EC CERTIFICATE</b> Examen de Type / Type - Examination ANNEXE III Directive 93/42/CEE relative aux dispositifs médicaux ANNEX III DIRECTIVE 93/42/EEC concerning medical devices					
Fabricant (nom et adresse) <i>Manufacturer (name and address)</i>	EFS ELECTRONIQUE ZAC du Baconnet 69700 MONTAGNY FRANCE				
Catégorie du(des) dispositif(s) <i>Device(s) category</i>	Appareil de traitement pour l'hyperthermie intracavitaire (pupitre de commande) <i>Equipment for intracavitary hyperthermia treatment (console)</i>				
Identification du(des) dispositif(s) <i>Identification of device(s)</i>	CAVITHERM				
<small>Le LNE/G-MED atteste qu'à l'examen des résultats figurant dans le rapport référencé 60001712, un échantillon représentatif de la production est conforme aux exigences de l'annexe I de la Directive 93/42/CEE. LNE/G-MED certifies that, on the basis of the results contained in the file referenced 60001712, a representative sample of the production complies with the requirements of the Directive 93/42/EEC, annex I.</small>					
<b>Cette attestation est valable jusqu'au : 16 octobre 2006 (inclus)</b> <i>This certificate is valid until : October 16<sup>th</sup>, 2006 (included)</i>					
<table border="1"><tr><td>LNE/G-MED</td><td>CE</td><td>0459</td></tr></table>		LNE/G-MED	CE	0459	 <b>Pour Le Directeur Général</b> <b>For General Director</b> Laurence DAGALLIER Directeur Certification Certification Director
LNE/G-MED	CE	0459			
<small>B3</small>		<small>2004-12-16</small>			
<small>LABORATOIRE NATIONAL D'ESSAIS • Établissement Public à Caractère Industriel et Commercial LNE/G-MED • Organisme notifié n° 0459 1, rue Gaston Boissier 75724 Paris Cedex 15 • Tél. 01 40 43 37 00 • 01 40 43 39 78 • Fax 01 40 43 37 37 • Internet : www.gmed.fr</small>					

# Key Points to Remember

- **A device never acts alone. The components of a device-related system include:**
  - The device**
  - The family**
  - The patient**
  - The operator**
  - The environment**
- **Reportable events involving medical devices must be reported to the Food and Drug Administration and the manufacturer within ten working days.**
- **Bio-Medical Engineering, Materials Management and Risk Management collaborate in preparing these reports.**



**THANK YOU FOR YOUR ATTENTION**

