Contaminación externa de viales: evaluación de actuaciones

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ClinicalOncology news

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Safe Handling Of Hazardous Drugs:

Reviewing Standards for Worker Protection

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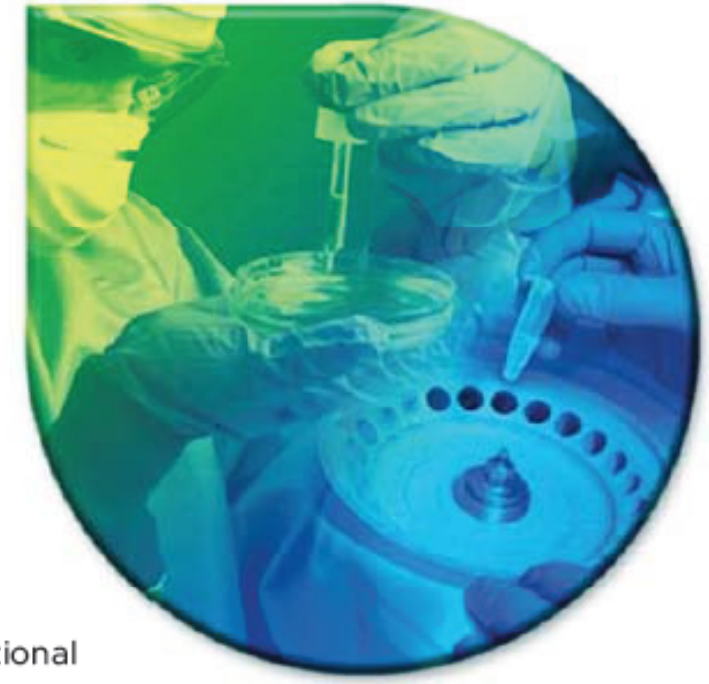

The year 2010 marks 3 decades of concern for health care workers exposed to cytotoxic and other hazardous drugs. As a new generation of health care workers joins those already engaged in patient care, it is essential that they understand the occupational risks associated with the handling of hazardous drugs and the need for training in proper techniques for all handling activities to reduce occupational exposure to such drugs.

CRONOLOGIA

- Finales de los 70 se reconoce por primera vez la exposición ocupacional a fármacos peligrosos y el potencial riesgo para la salud de los trabajadores

- Desde 1980 aparición de guias y recomendaciones para la manipulación segura:

  - Occupational Safety and Health Administration (OSHA): 1986, 1995, 1999.
  - American Society of Health-System Pharmacists (ASHP): 1985, 1990, 2006.
  - ISOPP Standars Practice. Safe Handling of Cytotoxics. ISOPP Standars Practice. Safe Handling of Cytotoxics: 2007.
  - National Institute for Occupational Safety and Health (NIOSH):2004
  - United States Pharmacopeia (USP): 2007. Chapter <797> "Pharmaceutical Compounding-Sterile Preparations". Incluye un apartado específico de fármacos peligrosos. Se considera un "**estandar**" y establece como requerimientos muchas de las recomendaciones de la NIOSH

GUIDELINES/RECOMENDACIONES

- ASHP Guidelines on Handling Hazardous Drugs. Am J Health-Syst Pharm. 2006;63:1172-93.
- Controlling occupational exposition exposure to hazardous drugs. En: OSHA technical manual. www.osha-slc.gov
- NIOSH Alert: Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Healthcare Settings. Department of Health and Human Services. CDC 2004.
- Cajaraville G, Tamés MJ. Guía de manejo de medicamentos citostáticos. Sanidad y Ediciones SL, 2002
- Agentes citostáticos. Comisión de Salud Pública. Consejo Interterritorial del Sistema Nacional de Salud. 2003
- NTP Instituto Nacional de Seguridad e Higiene en el Trabajo. Ministerio de Trabajo y Asuntos Sociales.
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- Cytotoxic Agents, Safe Handling Standards. British Columbia Cancer Agency. 2000
- International Agency for Research on Cancer. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans:Pharmaceutical Drugs. Lyon, France:IARC;2000.
- Polovich M, Power LA. Safe Handling of Hazardous Drugs. Special Report 2005
- Safe Handling of cytotoxic drugs. Health and Safety Executive HSE. www.hse.gov.uk 2003
- Preparation of Cytotoxic Drug Products. Professional Practice Standards. Pharmaceutical Society of Australia. Version 3. 2006. www.psa.org.au
- ISOPP Standars Practice. Safe Handling of Cytotoxics. J Oncol Pharm Practice 2007; Supplement 13:1-81.

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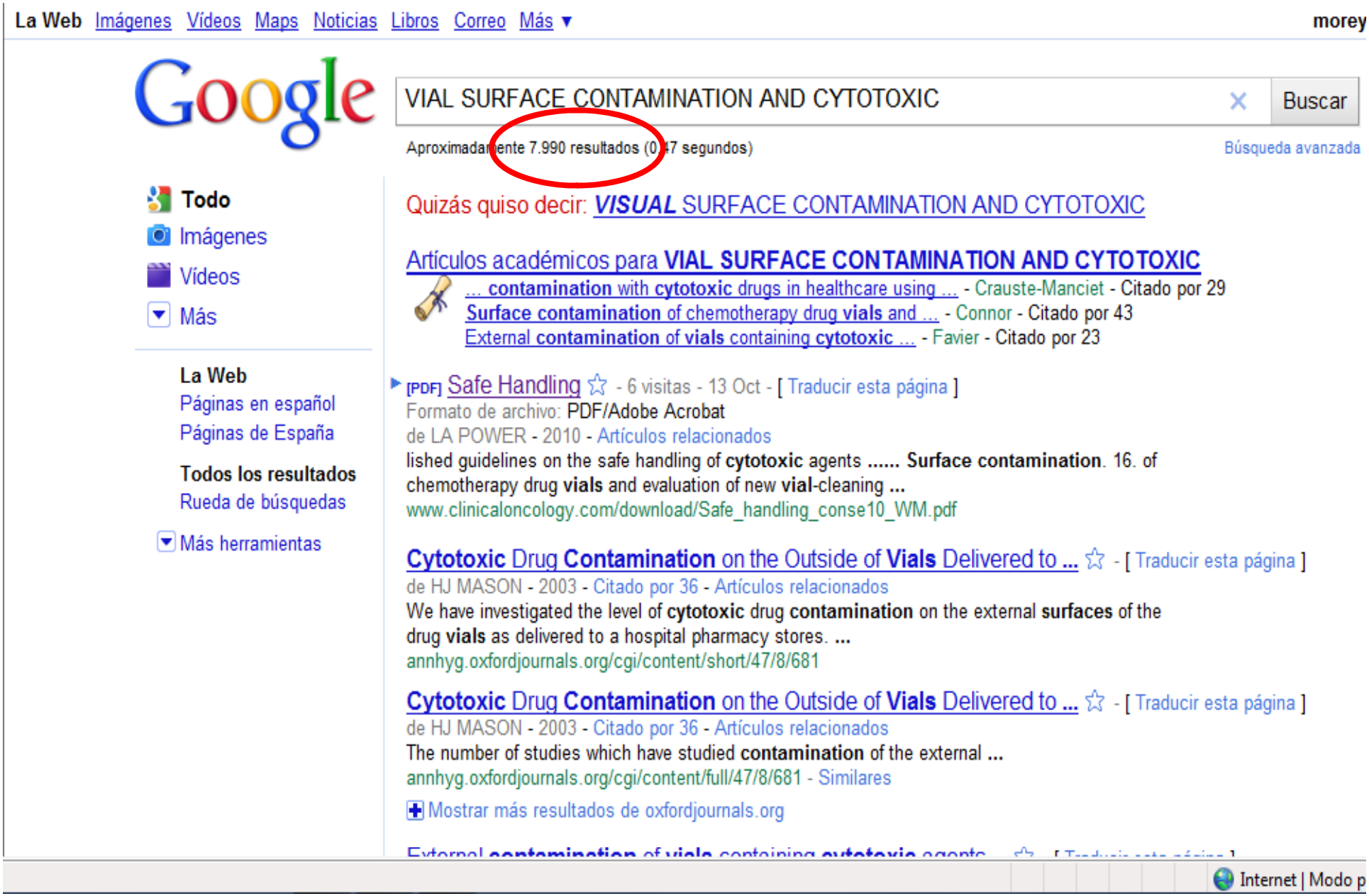
- Tanimura M, Yamada K, Sugiura S, et al. An environmental and biological study of occupational exposure to Cyclophosphamide in the pharmacy of a Japanese Community Hospital designated for the treatment of cancer. Journal of Health Science 2009; 55(5):750-56.

- **Principales vías de exposición de los manipuladores:**
  - Exposición dérmica: por contacto con superficies contaminadas
  - Inhalación: partículas y vapores

- **Principales fuentes de contaminación:**
  - Producción de aerosoles por manipulación inadecuada
  - Obertura de ampollas
  - Retirada de aguja del vial
  - Salpicaduras
  - Derrames
  - **Contaminación de superficie externa de viales**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VIAL SURFACE CONTAMINATION AND CYTOTOXIC
Buscar
Aproximadamente 7.990 resultados (0,47 segundos)
Búsqueda avanzada
Todo
Imágenes
Vídeos
Más
La Web
Páginas en español
Páginas de España
Todos los resultados
Rueda de búsquedas
Más herramientas
Quizás quiso decir: VISUAL SURFACE CONTAMINATION AND CYTOTOXIC
Artículos académicos para VIAL SURFACE CONTAMINATION AND CYTOTOXIC
... contamination with cytotoxic drugs in healthcare using ... - Crauste-Manciet - Citado por 29
Surface contamination of chemotherapy drug vials and ... - Connor - Citado por 43
External contamination of vials containing cytotoxic ... - Favier - Citado por 23
[PDF] Safe Handling - 6 visitas - 13 Oct - [Traducir esta página]
Formato de archivo: PDF/Adobe Acrobat
de LA POWER - 2010 - Artículos relacionados
lished guidelines on the safe handling of cytotoxic agents ..... Surface contamination. 16. of chemotherapy drug vials and evaluation of new vial-cleaning ...
www.clinicaloncology.com/download/Safe_handling_conse10_WM.pdf
Cytotoxic Drug Contamination on the Outside of Vials Delivered to ... - [Traducir esta página]
de HJ MASON - 2003 - Citado por 36 - Artículos relacionados
We have investigated the level of cytotoxic drug contamination on the external surfaces of the drug vials as delivered to a hospital pharmacy stores. ...
annhyg.oxfordjournals.org/cgi/content/short/47/8/681
Cytotoxic Drug Contamination on the Outside of Vials Delivered to ... - [Traducir esta página]
de HJ MASON - 2003 - Citado por 36 - Artículos relacionados
The number of studies which have studied contamination of the external ...
annhyg.oxfordjournals.org/cgi/content/full/47/8/681 - Similares
Mostrar más resultados de oxfordjournals.org
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CONTAMINACIÓN DE VIALES COMERCIALES

Referéncia		Citostátic	ng/cm²
Nygren (2002)	Viales	Cisplatino	0,2-99 (en total)
	Tapones	Cisplatino	0,6-21 (en total)
Favier (2003)	Viales	Etopósido	2,9-18,5
		5-Fluorouracilo	2,5-15,3
		Ifosfamida	0,1
		Ciclofosfamida	<0,1-0,1
		Doxorubicina	<0,1-0,2
	Envase exterior	5-Fluorouracilo	0,5
		Etopósido	ND
Mason (2003)	Viales	Carboplatino	7-251 (en total)
		Cisplatino	ND-9 (en total)
		Ciclofosfamida	ND-39 (en total)
		Ifosfamida	ND-344 (en total)
		Metotrexato	ND-18 (en total)
Edmer (2005)	Envase exterior	Ciclofosfamida	0,5-3,2 (en total)
		Ifosfamida	ND-10 (en total)
	Viales	Ciclofosfamida	13-19 (en total)
		Ifosfamida	1,6-24 (en total)
Schulz (2005)	Viales	Ciclofosfamida	0,5-2,89
Rosell* (2006)	Viales	Ciclofosfamida	0,004-0,1
	Tapones		<0,001-0,5
	Envase exterior		<0,001

EXPERIENCIA ICO

Punto de partida año 2005: participación estudio y obtención de datos propios de contaminación por ciclofosfamida en superfícies

1._Medidas inmediatas adoptadas:

- ✓ Limpieza integral unidad con **NaOH 0,03 M**
- ✓ Limpieza diaria con NaOH 0,03 M
- ✓ Revisión CSB
- ✓ Trabajo continuado con mascarilla de protección respiratoria FFP3
- ✓ Cambio en sistema de eliminación de residuos
- ✓ Aumento en la frecuencia de las rotaciones

2._ Contacto con el equipo de prevención laboral Mancomunidad.

3._ Contacto con Instituto Nacional para la Seguridad y Higiene en el Trabajo (INSHT)

4._ Acciones:

- Revisión de caudales de impulsión y extracción de la unidad
- **Determinación de contaminación: viales y superficies**
- **Valoración de sistemas de limpieza**
- Valoración de métodos de trabajo
- Seguimiento

DETERMINACIÓN CONTAMINACIÓN:

Superficies

Muestras de superficies	CTX (ng/cm^2) 2006	CTX (ng/cm^2) 2005
CSB	ND	1,38
Suelo delante CSB	0,097	1,67
Poyata 1	0,094	0,21
Poyata 2	ND	0,31

No detectable <0,001 ng/cm^2

Viales

Muestras de viales	CTX (rango)
V_1, V_2, V_3, V_4	0,42 – 10,8 ng
T_1, T_2	0,33 – 1,60 ng

No detectable <0,1 ng

ESTUDIO LIMPIEZA VIALES (I)

1ª PARTE:

- **Experimento contaminación viales:**
  - Dos métodos de contaminación de viales y dos soluciones de diferente concentración:
    - ✓ Deposición
    - ✓ Inmersión
  - Resultados:
    - Se detectó CTX en todos los casos
    - Se utilizó la disolución de menor concentración (simula mejor la cantidad de CTX encontrada en los viales comerciales)
    - La deposición con jeringa más sensible y reproducible

ESTUDIO LIMPIEZA VIALES (II)

2ª PARTE:

- Contaminación de viales por deposición con jeringa cromatográfica Hamilton de 10 μL de una disolución de CTX de 2,5 μg/mL.
  - Una vez contaminados los viales se limpian por inmersión durante 2 minutos en la solución de limpieza correspondiente.
  - Una vez secos se determina la CTX en la superficie de los viales mediante un frotis de la superficie exterior con un papel absorbente (Kleenex) impregnado con 1 mL de una solución de NaOH 0,03 M.

ESTUDIO LIMPIEZA VIALES (III)

- **Resultados:**

	Isopropanol	Etanol	Lejia	Virkon® (Persulfato potásico)	Agua	Jabón neutro	NaOH 0,03 M
1							
2							
3							
4							
5							
6							
Media %							
SD							

ESTUDIO LIMPIEZA VIALES (III)

- **Resultados:**

Porcentaje (%) de Recuperación de Ciclofosfamida del vial una vez limpiado

	Isopropanol	Etanol	Lejia	Virkon® (Persulfato potásico)	Agua	Jabón neutro	NaOH 0,03 M
1	18,2	16,7	4	1,5	2,1	0	0
2	20,9	80,2	0	1,4	0	2,6	0
3	16,2	7,5	0	1,3	0	0	0
4	17	8,9	6,7	1,4	2,7	0	0
5	30,8	7,5	0	2	0	0	0
6	70,5	4,3	0	1,4	0	0	0
Media %	28,9	20,9	1,8	1,5	0,8	0,4	0
SD	21,1	29,4	2,9	0,2	1,3	1	0

Contacto con Baxter

Baxter

Date: **2007-11-08**
P. Böddeker

Correspondence

To whom it may concern.

Outer contamination of Cytostatics

Baxter Oncology manufactures alkylating cytostatics since the early 50's and has gained a lot of experience with these products.
Our cytostatics are manufactured in our plant for parenterals in Halle (Germany). The cytostatics are produced in dedicated areas. We use an isolator filling line for the filling of powder products (ifosfamide). The bulk sterile dry substance ifosfamide is filled into vials on this isolator powder filling line. During the filling process the individual vials are filled from the vessel via an exhausting connection, so the powder cannot by pass the vial mouth. The filling process is only initiated when an empty vial is confirmed in the correct filling position (sensor). After the filling process the vials are closed with a stopper and sealed with a metal crimp. Cyclophosphamide vials are produced via freeze-drying of the liquid vials. The next step in case of both products is an outer washing step with purified water on Seidenader DAR 350 washing machines. According to our information Baxter Oncology was one of the first companies introducing an outer washing process of powder filled vials in 1989. The vials are then inspected for visible defects and outer contamination.
Some years ago we checked the outer contamination of vials after the washing process and didn't detect contamination with respect to the limit of detection of the analytical method.
With a much more sensitive analytical method (Gaschromatography with mass spectrometer) we have found contamination in the low µg and nanogram range in the past. To further reduce the level of outer contamination we installed the newest generation type Seidenader DAR 350.
The cleaning machines and the washing process were qualified with a suitable substance. Cleaning effectiveness was checked during the routine production of cytostatics.
Nevertheless we cannot assure that there is no contamination on the outside of the vials. There are even other risks during transport and handling, where contamination may occur. Furthermore analytical results are always limited to the sensitivity of the analytical methods applied.
We think that we have taken protective measures, which are state of the art against outer contamination. If our customers follow the legal requirements and the recommendations for the handling of cytotoxics we would expect that the handling of our products is safe.

Baxter Oncology GmbH

Peter Böddeker,
Director Quality Management

Production of Parenteral Cytotoxics
Isolator Technology

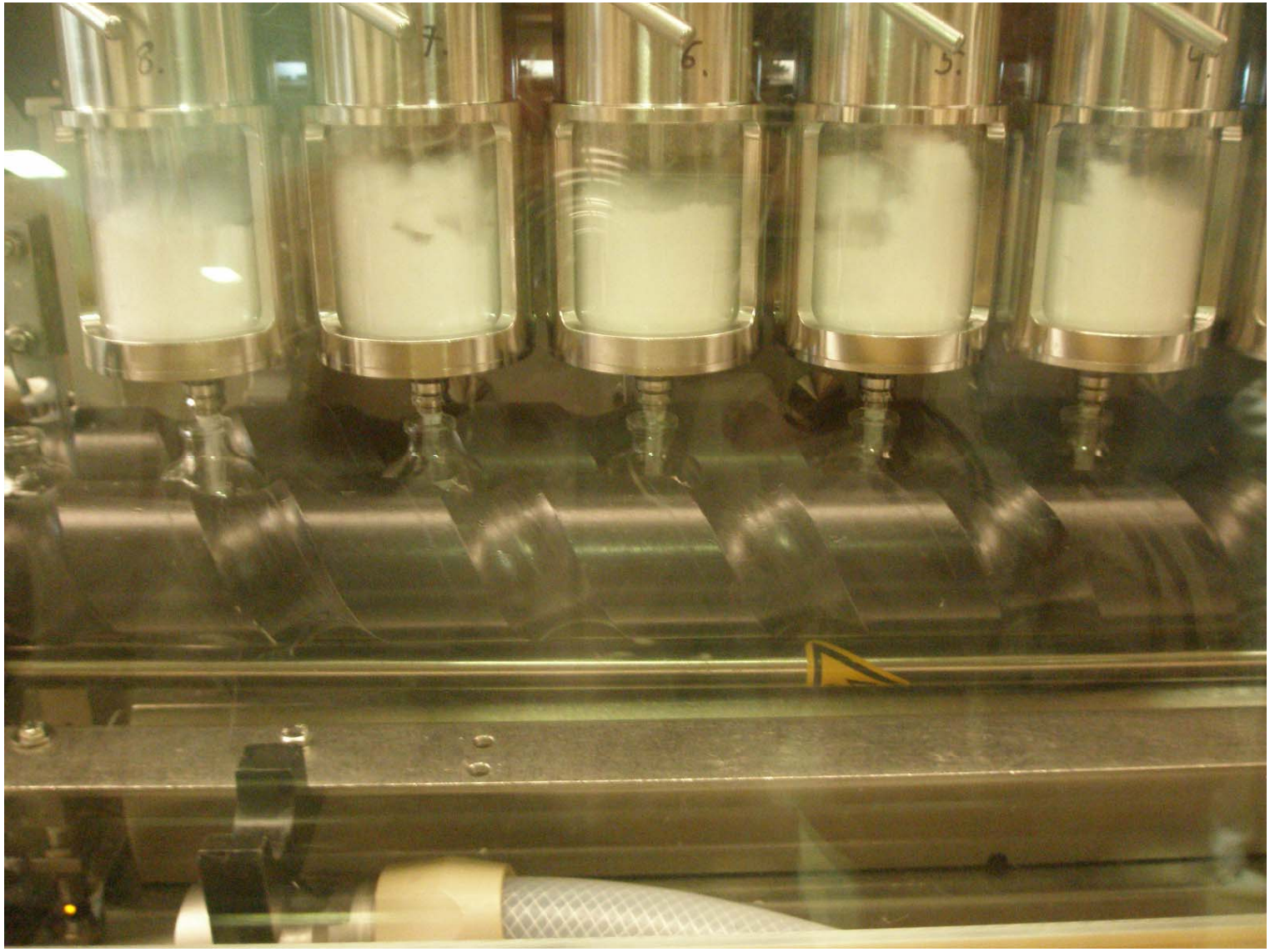
Presentation Barcelona
2008-03-10

Limpieza viales vacíos

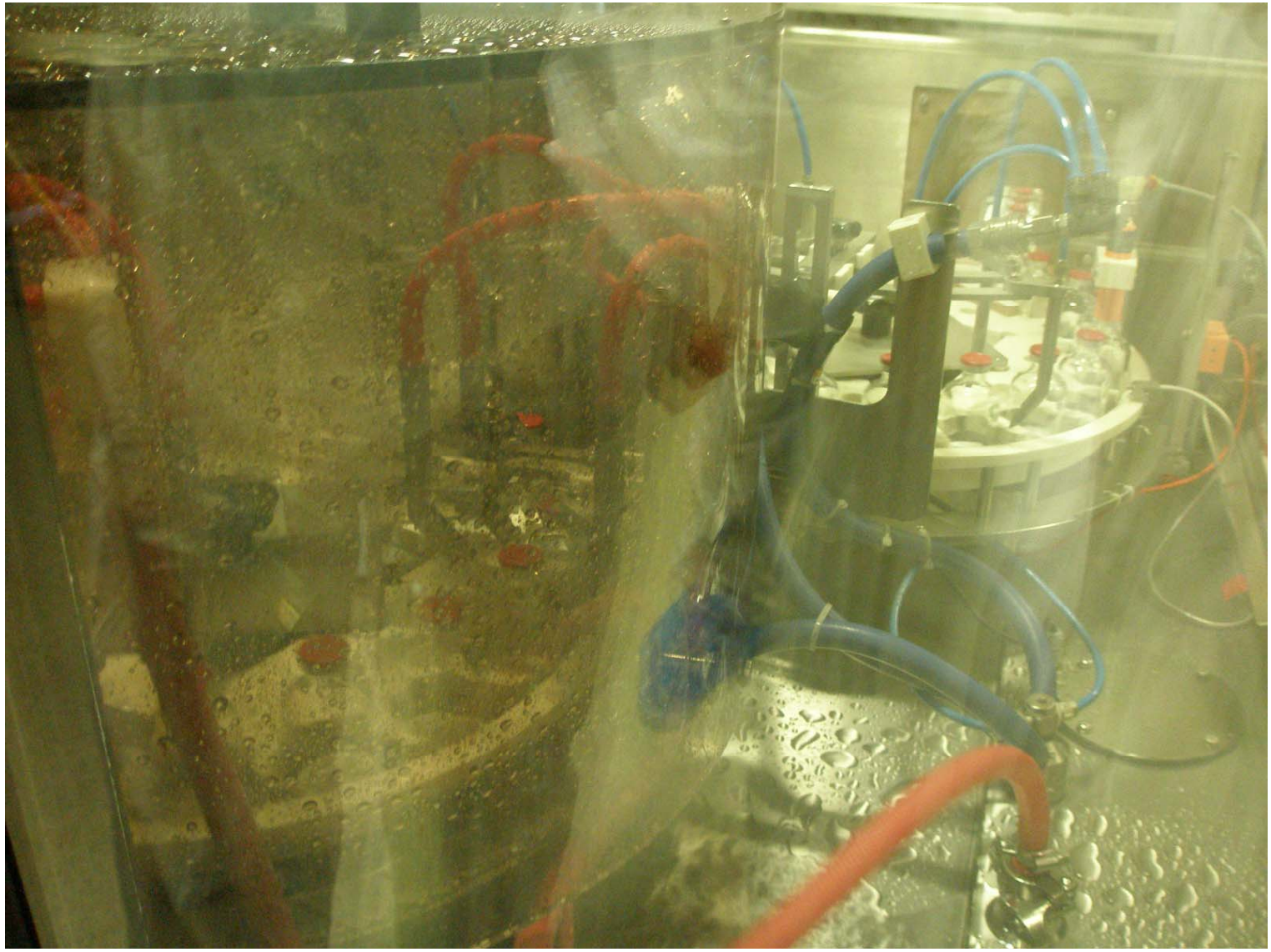
Secado viales vacíos

Zona de llenado

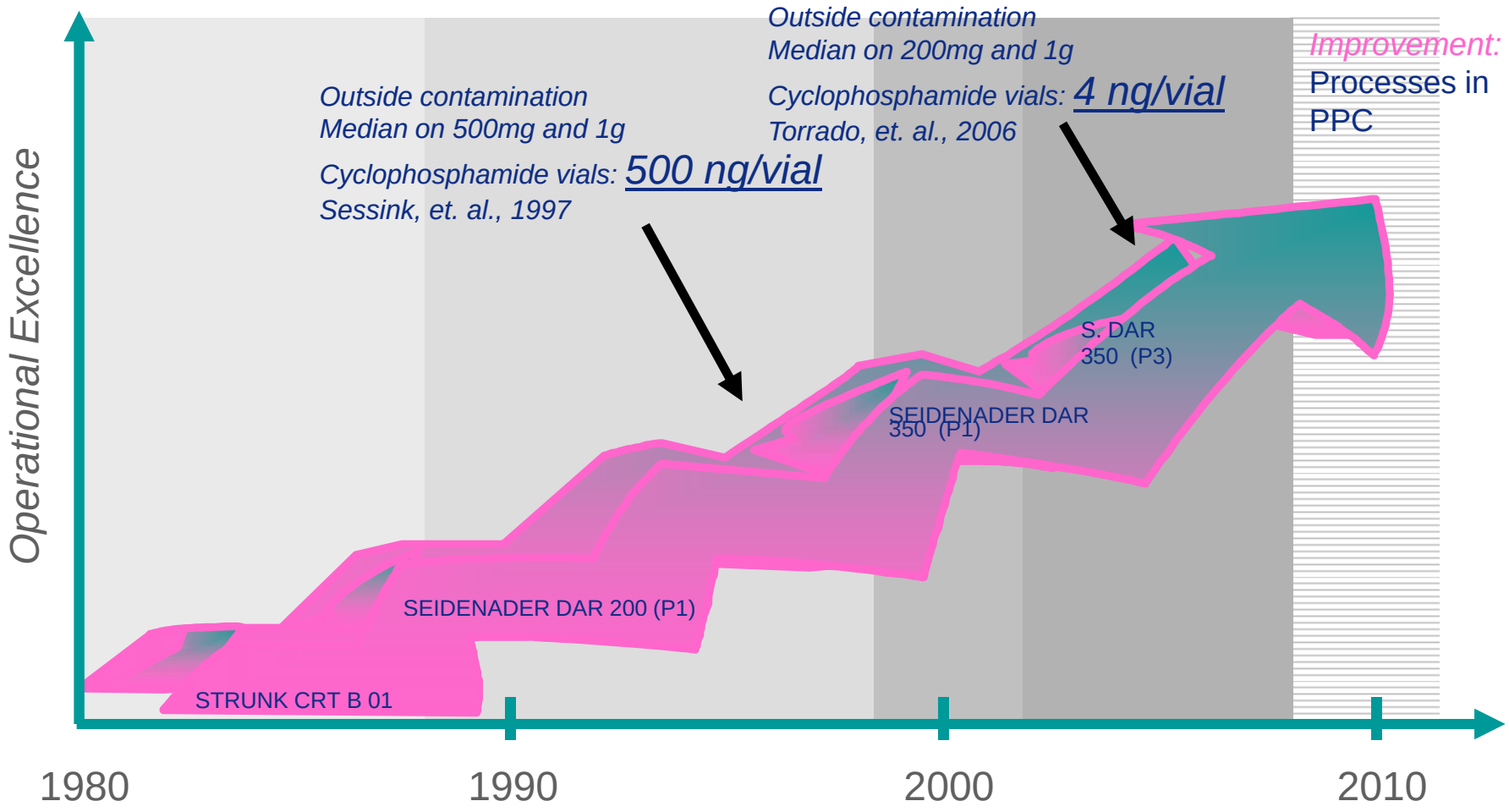
Llenado viales



Limpieza y secado viales llenos



Continuous Improvement



LINEAS DE TRABAJO

- Sistema de lavado de viales de ciclofosfamida
- Plantear una sistemática de monitorización de la contaminación en superficies

¡Los niveles mínimos de contaminación aceptables todavía no se han determinado !!!! USP < 1 ng/cm^2

ESTUDIO LIMPIEZA VIALES (I)

1ª PARTE:

- **Experimento para determinar el tiempo óptimo de lavado:**
  - Contaminación de viales mediante deposición con jeringa:
    - ✓ 6 viales para cada tiempo de limpieza: 8, 20, 28 minutos sin jabón y 28 minutos con jabón
    - ✓ 6 viales sin limpiar
  - Una vez contaminados se limpian en el lavaplatos
  - Se dejan secar y se realiza la toma de muestras en la superficie
  - Los viales no limpiados se utilizan como referencia para determinar el porcentaje de recuperación

ESTUDIO LIMPIEZA VIALES (II)

1ª PARTE:

- **Resultados:**
  - No se detecta presencia de ciclofosfamida en ninguno de los viales limpiados en el lavaplatos
  - Con los cuatro programas estudiados se obtiene una limpieza del 100%
  - Se decide utilizar el programa más corto sin jabón

ESTUDIO LIMPIEZA VIALES (III)

2ª PARTE:

- **Limpieza de viales comerciales**
  - Se determinó la presencia de ciclofosfamida en viales comerciales de 2 lotes diferentes
  - 3 viales de cada lote se limpian con el programa elegido
  - 3 viales se analizan sin limpiar
  - La toma de muestras se realizó mediante frotis por duplicado de la superficie del vial con un papel absorbente, impregnado con 1 mL de una solución de NaOH 0.03 M

ESTUDIO LIMPIEZA VIALES (IV)

2ª PARTE:

- **Resultados:**
  - En los viales comerciales sometidos a limpieza no se detectó presencia de ciclofosfamida
  - Cantidad detectada en viales sin limpiar:

Lote	Vial	Ciclofosfamida
9K665	1	13 ng
	2	1.43 ng
	3	ND
0B673	1	ND
	2	1.43 ng
	3	ND

ND<1.43ng

LINEAS DE TRABAJO

- Evaluar si la limpieza de viales impacta en los niveles de contaminación de la unidad, para ello:
  - Realizar un basal previo al inicio de la limpieza sistemática de viales
  - Nueva toma de muestras después de un tiempo instaurado el lavado de viales
- Establecer un programa de monitorización de contaminación de superficies

CONCLUSIONES……:PREVENCIÓN

- Medidas para la reducción de contaminación en superficies:
  - EPIs: Guantes!!!!!!!
  - Control ambiental (cabinas, sala)
  - Técnica de preparación adecuada
  - Limpieza
  - Gestión de residuos
  - Plan de formación
  - Nuevas tecnologias

Table 4. Comparison of NIOSH, OSHA, ASHP, And USP Chapter <797> Recommendations for PPE

	NIOSH/OSHA	ASHP	USP Chapter <797>
General handling	• Use double gloving for all activities involving hazardous drugs. **OSHA:** • Protective equipment, including PPE for eyes, face, head, and extremities, protective clothing, respiratory devices, and protective shields and barriers shall be provided, used, and maintained in a sanitary and reliable condition wherever it is necessary by reason of hazards of processes or environment, chemical hazards, radiological hazards, or mechanical irritants encountered in a manner capable of causing injury or impairment in the function of any part of the body through absorption, inhalation, or physical contact.	• Wear double gloves for all activities involving hazardous drugs. • Guidelines for the safe handling of hazardous drugs recommend the use of gowns for compounding in the BSC, administration, spill control, and waste management to protect the worker from contamination by fugitive drug generated during the handling process.	• Hazardous drugs shall be handled with caution at all times with the use of appropriate chemotherapy gloves during receiving, distributing, stocking, taking inventory, preparing for administration, and disposal.

CONTAMINACIÓN DE GUANTES

Referencia	Citostático	Cantidad
CRAUSTE-MANCIET, S., SESSINK, P.J.M., FERRARI, S., JOMIER, J.-Y. Y BROSSARD, D. (2005). **Environmental Contamination with Cytotoxic Drugs in Healthcare Using Positive Aire Pressure Isolators.** ***Ann. occup. Hyg. 49 (7): 619-628.***	Ciclofosfamida	< 0,009 ng - 9 mg
	Ifosfamida	< 0,009 ng - 930 mg
	5-Fluorouracilo	< 1,8 ng - 359 mg
	Metotrexato	< 0.9 ng - 1,6 mg
ZIEGLER, E., MASON, H.J. Y BAXTER, P.J. (2002). **Occupational exposure to cytotoxic drugs in two UK oncology wards.** ***Occup. Environ. Med. 59: 608-612.***	Platino	< 1 ng - 36 mg
	Ciclofosfamida	ND-11.2
	Ifosfamida	ND - 1,8 mg
	Metotrexato	ND - 49.3 ng
SESSINK, P.J.M., VAN DE KERKHOF, M.C.A., ANZION, R.B.M., NOORDHOEK, J. Y BOS, R.P. (1994). **Environmental Contamination and Assessment of Exposure to Antineoplastic Agents by Determination of Cyclophosphamide in Urine of Exposed PharmacyTechnicians: Is Skin Absorption an Important Exposure Route?.** ***Arch. Environ Health 49 (3):165-169.***	Ciclofosfamida	< 80 ng - 9.6 mg
	5-Fluorouracilo	< 4 mg - 760 mg
	Metotrexato	<11 mg -1,9 mg
SESSINK, P.J.M., BOER, K.A., SCHEEFHALS, A.P.H., ANZION, R.B.M.Y BOS R.P. (1992). **Occupational exposure to antineoplastic agents at several departments in a hospital. Environmental contamination and excretion of cyclophosphamide and ifosfamide in urine of exposed workers.** ***Int. Arch. Occup. Environ. Health 64:105-112.***	Ciclofosfamida	<0.1 mg - 21 mg
	5-Fluorouracilo	19 mg - 87 mg
	Metotrexato	<6 mg - 49 mg

Table 2. Comparison of the NIOSH, ASHP, and USP Chapter <797> Recommendations for the Hazardous Drug Compounding Environment

	NIOSH	ASHP	USP Chapter <797>
Storage environment	Store hazardous drugs separately from other drugs in an area with sufficient general exhaust ventilation to dilute and remove any airborne contaminants.	Segregate hazardous drug inventory and store in an area with sufficient general exhaust ventilation to dilute and remove any airborne contaminants.	Hazardous drugs shall be stored separately from other inventory, preferably within a containment area such as a negative-pressure room.
Compounding	Prepare hazardous drugs in an area that is devoted to that purpose alone and is restricted to authorized personnel.	Hazardous drugs should be compounded in a controlled area where access is limited to authorized personnel trained in handling requirements.	Hazardous drugs shall be prepared in a PEC, which shall be placed in an ISO class 7 area that is physically separated from other preparation areas.
Ventilation	Where feasible, exhaust 100% of the filtered air to the outside.	Because of the hazardous nature of these preparations, a contained environment where air pressure is negative relative to that of the surrounding areas or that is protected by an air lock or anteroom is preferred.	*Storage:* area should have exhaust ventilation of at least 12 air changes per hour. *Compounding:* optimally at negative pressure relative to adjacent positive-pressure ISO class 7 or better ante-areas.

ASHP, American Society of Health-System Pharmacists; **ISO,** International Organization for Standardization; **NIOSH,** National Institute for Occupational Safety and Health; **PEC,** primary engineering control; **USP,** United States Pharmacopeia

DUDAS

- Soluciones de Limpieza
- Monitorización
- Límite de detección
- Limpieza de viales


¡¡GRACIAS!!

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CYTO WIPE KIT

to measure environmental contamination with the cytostatic drugs cyclophosphamide, ifosfamide, 5-fluorouracil and methotrexate.

Contents

This wipe kit contains the materials to take 6 wipe samples from several types of surfaces.

- 6 x 2 = 12 tissues
- 6 droppers with 17 ml 0.03 M NaOH (sodium hydroxide*) solution
- 6 containers including labels and plastic mini bags
- 6 pair of gloves

CYTO WIPE KIT

to measure environmental contamination with the cytostatic drug etoposide.

Contents

This wipe kit contains the materials to take 6 wipe samples from several types of surfaces.

- 6 x 2 = 12 tissues
- 6 droppers with 17 ml 50% ethanol*/water
- solution
- 6 containers including labels and plastic mini bags
- 6 pair of gloves
- registration form
- label with the address of the lab of Exposure Control

CYTO WIPE KIT

to measure environmental contamination with the cytostatic drug mitomycine C.

Contents

This wipe kit contains the materials to take 6 wipe samples from several types of surfaces.

- 6 x 2 = 12 tissues
- 6 droppers with 17 ml water (aqua pure*)
- 6 containers including labels and plastic mini bags
- 6 pair of gloves
- registration form
- label with the address of the lab of

CYTO WIPE KIT

to measure environmental contamination with the cytostatic drugs cis-platin and carboplatin.

Contents

This wipe kit contains the materials to take 6 wipe samples from several types of surfaces.

- 6 x 2 = 12 tissues
- 6 droppers with 17 ml 0.5 M HCl
- (hydrochloric acid*) solution
- 6 containers including labels and plastic mini bags
- 6 pair of gloves
- registration form
- label with the address of the lab of

gia