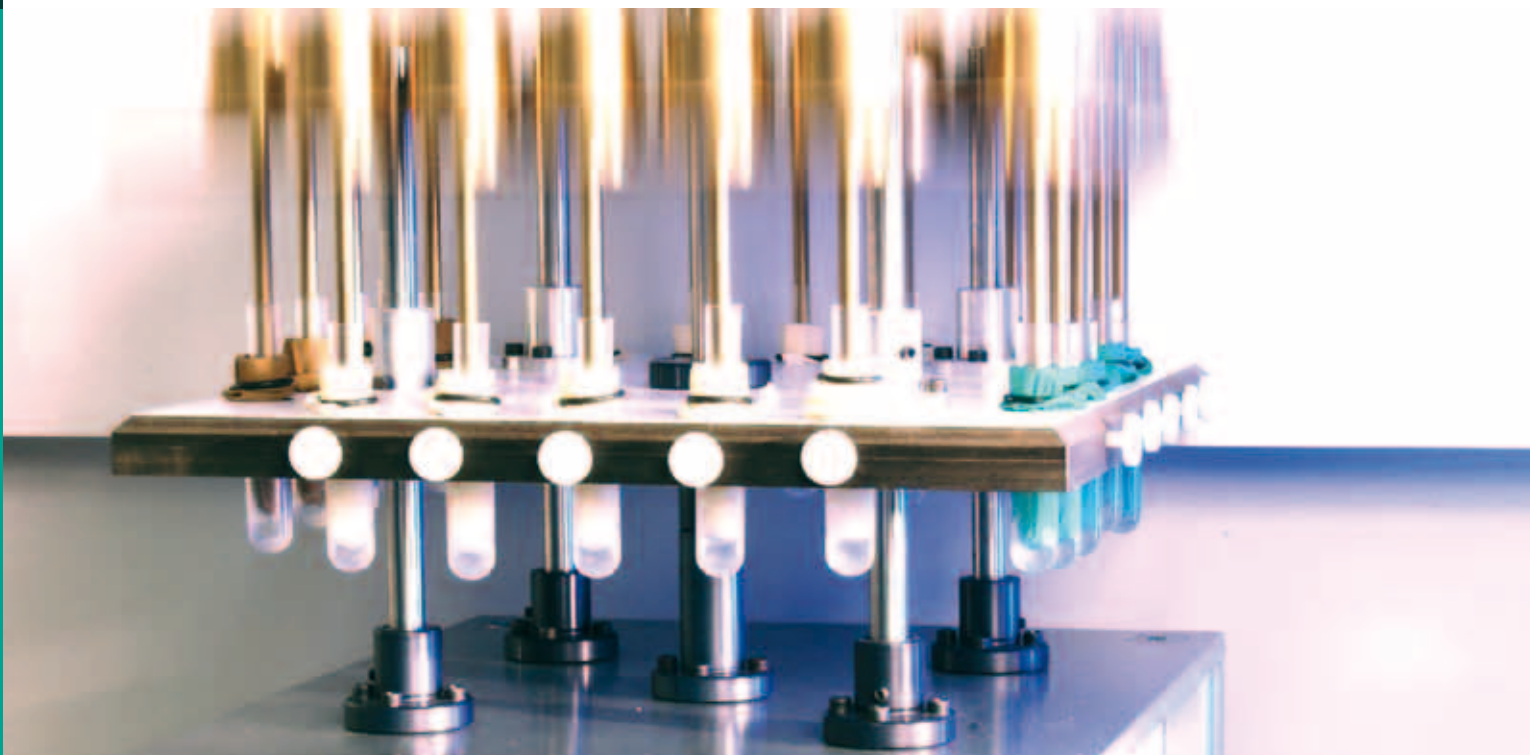


ACPP: Anell Cytostatic Permeation Program

Ansell invests for your protection and information



In partnership with the
Université Catholique de Louvain
Brussels - Belgium

Ansell

Why the ACPPE?

According to the World Health Organization, between now and 2020 the cancer rate is going to increase by 50 % to about 15 million new cases a year worldwide.

This predicted sharp increase in new cases will mainly be due to the existence of steadily ageing populations in both developed and developing countries, but also to the current prevalence of smoking and the rise in numbers of those adopting unhealthy lifestyles.

One of the most frequently used treatments for cancer is chemotherapy. Unfortunately it is well known that cytostatic agents are potentially hazardous for the manipulator.

Cytostatics are known to be:

- Mutagenic
- Carcinogenic
- Teratogenic.

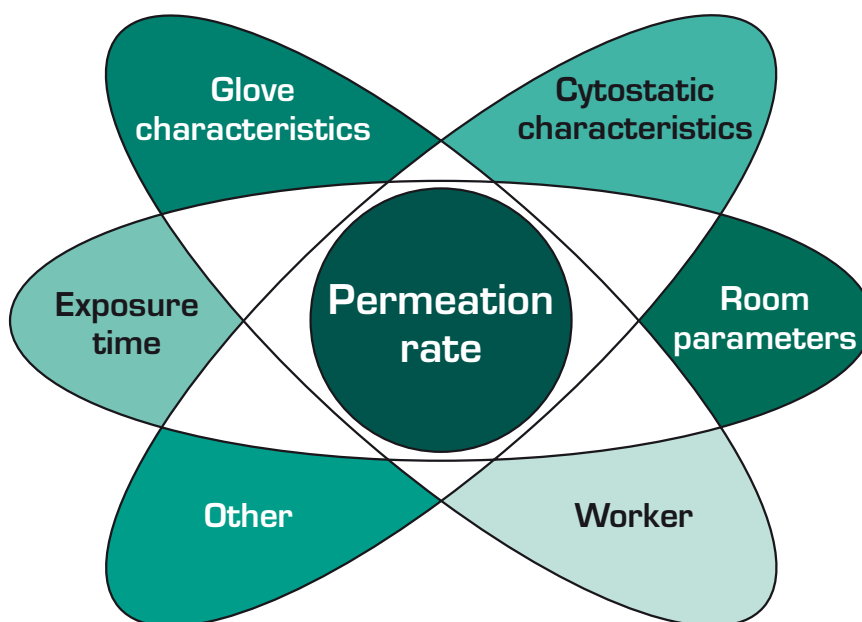
Some of the other potential effects are:

- Decrease in fertility
- Foetal malformation
- Miscarriage
- Extra uterine pregnancy
- High toxicity for certain organs.

ACPP project goals:

- To contribute to better protection for healthcare personnel handling cytostatics
- To present results corresponding to real life conditions or, better still, to worst case scenarios (dynamic treatment & cytostatic concentration)
- To be innovative & bring very practical answers to our customers

Permeation: a very complex process



Permeation depends on many parameters and therefore the results obtained cannot be extended to any other material, brand or competitive product.

Personal Protective Equipment by Ansell		Natural Rubber Latex			Synthetic	
		Sterile/Handspecific			Non-Sterile	
		Gammex® PF XP (NRL)	Gammex® PF XP™ tested after alcohol desinfection	DermaShield® (Neoprene)	NitraTouch® (Nitrile)	* NitraTex® & NitraTex® EP (Long Cuff) (Nitrile)
15 min	Carmustine	3	3	4	2	3
	Cisplatin	6	6	6	3	6
	Cyclophosphamide	6	6	6	4	6
	Cytarabine	6	6	6	6	6
	Docetaxel	6	6	6	6	6
	Doxorubicin	6	6	6	6	6
	Etoposide	6	6	6	6	6
	5-Fluorouracil	6	6	6	3	6
	Ifosfamide	5	5	6	4	4
	Irinotecan	6	6	4	4	5
	Methotrexate	6	6	6	4	6
	Mitomycin C	6	6	6		
	Oxaliplatin	6	6	6		
	Paclitaxel	6	6	6		
	Thiotepa	6	6	6	5	6
	Vinorelbine	6	6	4	6	4
Ganciclovir *	6	6	6			
30 min	Carmustine	2	2	3	2	3
	Cisplatin	3	3	6	3	6
	Cyclophosphamide	5	4	5	4	4
	Cytarabine	5	4	4	6	6
	Docetaxel	5	5	5	5	5
	Doxorubicin	6	5	6	4	6
	Etoposide	6	6	6	2	6
	5-Fluorouracil	6	6	6	3	6
	Ifosfamide	4	4	4	4	4
	Irinotecan	4	4	4	4	5
	Methotrexate	6	6	5	4	5
	Mitomycin C	6	6	4		
	Oxaliplatin	4	4	6		
	Paclitaxel	4	4	4		
	Thiotepa	5	5	5	5	6
	Vinorelbine	6	6	4	6	4
Ganciclovir *	5	5	5			
60 min	Carmustine	1	2	3	2	3
	Cisplatin	3	3	6	3	6
	Cyclophosphamide	5	5	5	4	3
	Cytarabine	5	5	4	6	5
	Docetaxel	5	5	5	4	5
	Doxorubicin	5	5	6	4	6
	Etoposide	4	4	4	2	6
	5-Fluorouracil	6	6	6	3	6
	Ifosfamide	4	4	4	4	4
	Irinotecan	4	4	4	3	5
	Methotrexate	6	6	5	4	5
	Mitomycin C	5	5	4		
	Oxaliplatin	4	4	4		
	Paclitaxel	4	4	4		
	Thiotepa	4	4	5	5	5
	Vinorelbine	6	6	4	5	4
Ganciclovir *	4	4	4			

Permeation temperature indicator: 25°C 37°C 43°C

*NitraTex® is a medical device for the delivery to the patient

Key to Protection level

Level 1 : Permeation detected up to 10 times below EN374-3 limit requirement

Level 2 : Permeation detected 10 to 100 times below EN374-3 limit requirement

Level 3 : Permeation detected 100 to 1.000 times below EN374-3 limit requirement

Level 4 : Permeation detected 1.000 to 10.000 times below EN374-3 limit requirement

Level 5 : Permeation detected 10.000 to 100.000 times below EN374-3 limit requirement

Level 6 : > Permeation detected at least 100.000 times below EN374-3 limit requirement or no permeation measured

Dynamic permeation levels based on ACPD vs those allowed by the existing norms

PRACTICAL EXAMPLE

Glove : Gammex® PF XP™ latex powder-free protective glove

Cytostatic drug : cyclophosphamide

Permeation time : 30 min

- Maximum permeation level allowed by EN374-3 : 1 µg/(cm² X min)
- Dynamic Permeation level according to ACPD testing procedure : 0,00009 µg/(cm² X min)
- Difference :
 $1,00000 / 0,00009 = 11.111$

ACPD data show that Gammex® PF XP™'s permeation level to cyclophosphamide after 30 min is 11.111 times inferior to the maximum level that European regulation allows.

Permeation levels allowed by the existing norms

EN374-3 : 2003 — *NOT SPECIFIC*

- “Protective gloves against chemicals and micro-organisms”.
Part 3: Determination of resistance to permeation by chemicals
- Limit is 1 µg (= 1.000 ng)/(cm² X min)

ASTM F 739-99a (June 1999) — *NOT SPECIFIC*

- “Standard test method for resistance of protective clothing materials to permeation by liquids or gases under conditions of continuous contact”.
- Limit is 0,1 µg (= 100 ng)/(cm² X min)

ASTM D 6978-05 (April 2006) — *SPECIFIC*

- “Practice for Assessment of Resistance of Medical Gloves to Permeation by Chemotherapy Drugs”.
- Limit is 0,01 µg (= 10 ng)/(cm² X min)

Details about analytical conditions are available upon request.

Neither this document nor any other statement made herein by or on behalf of Ansell should be construed as a warranty of merchantability or that any Ansell product is fit for a particular purpose. Ansell assumes no responsibility for the suitability or adequacy of an end user's selection of gloves for a specific application.

Dynamic Permeation Device

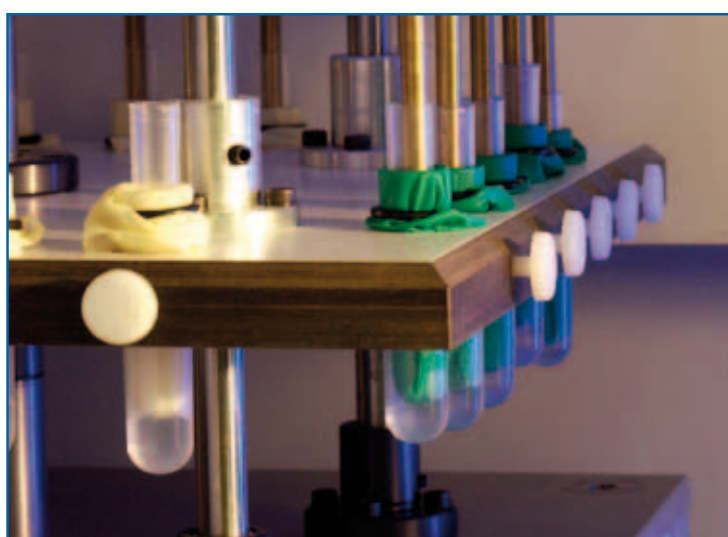
In order to ensure your maximum protection when handling cytostatics, Ansell has invested in a totally new permeation assessment protocol.

Because gloves are made to be used under dynamic physical conditions (stretching, tension,

rubbing etc.) we thought at Ansell that it was our duty to test some of our products for cytostatic permeation under the same constraints.

In partnership with the Université Catholique de Louvain, Brussels, Belgium, we have developed a UNIQUE

dynamic permeation device. After dynamic permeation simulation, aliquots of the collecting medium are analysed by LC-MS/MS (*1) or HPLC-DAD (*2)



Dynamic permeation device



The molecules tested are the following

	Cytostatic	Brand name	Company	Analytical method	Concentration	LOD (Detection limit)	LOQ (Quantification limit)	Mol. Weight	Log P
1	Carmustine	Nutrimon BICNU	Almirall-Prodesfarma	HPLC-DAD	3.0 mg/ml	59.02 ng/ml	196.73 ng/ml	214.0	1.50
2	Cisplatin	Platinol	Bristol-Myers Squibb	HPLC-DAD	1.0 mg/ml	49.70 ng/ml	165.67 ng/ml	300.1	- 2.20
3	Cyclophosphamide	Endoxan	AstaMedica	LCMS/MS	20.0 mg/ml	1.95 ng/ml	31.60 ng/ml	261.1	0.60
4	Cytarabine	Cytosar	Pharmacia & UpJohn	LCMS/MS	100.0 mg/ml	0.97 ng/ml	4.93 ng/ml	243.2	- 2.50
5	Docetaxel	Taxotere	Aventis Pharma	LCMS/MS	10.0 mg/ml	3.11 ng/ml	17.32 ng/ml	807.8	NA
6	Doxorubicin	Adriblastina	Pharmacia	LCMS/MS	2.0 mg/ml	35.26 ng/ml	55.10 ng/ml	543.5	1.30
7	Etoposide	Vepesid	Bristol-Myers Squibb	HPLC-DAD	20.0 mg/ml	63.06 ng/ml	210.19 ng/ml	588.5	0.60
8	5-Fluorouracil	Fluoroblastine	Pharmacia & UpJohn	HPLC-DAD	50.0 mg/ml	37.47 ng/ml	124.92 ng/ml	130.1	- 1.00
9	Ifosfamide	Holoxan	AstaMedica	LCMS/MS	100.0 mg/ml	4.11 ng/ml	45.11 ng/ml	261.1	NA
10	Irinotecan	Campto	Aventis Pharma	LCMS/MS	20.0 mg/ml	16.32 ng/ml	30.73 ng/ml	586.6	NA
11	Methotrexate	Ledertrexate	Wyeth Lederle	LCMS/MS	25.0 mg/ml	1.41 ng/ml	12.85 ng/ml	454.4	- 1.80
12	Thiotepa	Ledertepa	AstaMedica	LCMS/MS	10.0 mg/ml	3.06 ng/ml	17.36 ng/ml	189.2	0.50
13	Vinorelbine	Navelbine	Pierre Fabre	LCMS/MS	10.0 mg/ml	6.48 ng/ml	43.72 ng/ml	779.9	16.00
14	Mitomycin C	Mitomycin C	Nycomed Belgium	HPLC-DAD	0.4 mg/ml	12.80 ng/ml	42.50 ng/ml	318.0	NA
15	Oxaliplatin	Eloxatin	Sanofi-Synthelabo	HPLC-DAD	5.0 mg/ml	19.00 ng/ml	64.00 ng/ml	397.3	NA
16	Paclitaxel	Taxol	Bristol-Myers Squibb	HPLC-DAD	6.0 mg/ml	37.50 ng/ml	125.00 ng/ml	853.9	NA
17	Ganciclovir (*3)	Cymevene	Roche	LCMS/MS	50.0 mg/ml	6.00 ng/ml	20.00 ng/ml	255.2	- 1.60

(*1) LC-MS/MS: Liquid Chromatography Tandem Mass Spectrometry

(*2) HPLC -DAD: High Pressure Liquid Chromatography - Diode Array Detection

(*3) Anti-viral drug

Permeability of 13 different gloves to 13 cytotoxic agents under controlled dynamic conditions



PIERRE E. WALLEMACQ, ARNAUD CAPRON, ROGER VANBINST,
ERIC BOECKMANS, JEAN GILLARD, AND BERTRAND FAVIER

The ACPP methodology & results were recently published on March 15th 2006
in the American Journal of Health-System Pharmacy (AJHP).

Ansell

Ansell Limited is a global leader in barrier protective products. With operations in the Americas, Europe and Asia, Ansell employs more than 11,000 people worldwide and holds leading positions in the natural latex and synthetic polymer glove and condom markets. Ansell operates in three main business segments: Occupational Healthcare, supplying hand protection to the industrial market; Professional Healthcare, supplying surgical and examination gloves to healthcare professionals; and Consumer Healthcare, supplying condoms and consumer hand protection.

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