Pathogen inactivation in transfusion plasmas (Intercept)

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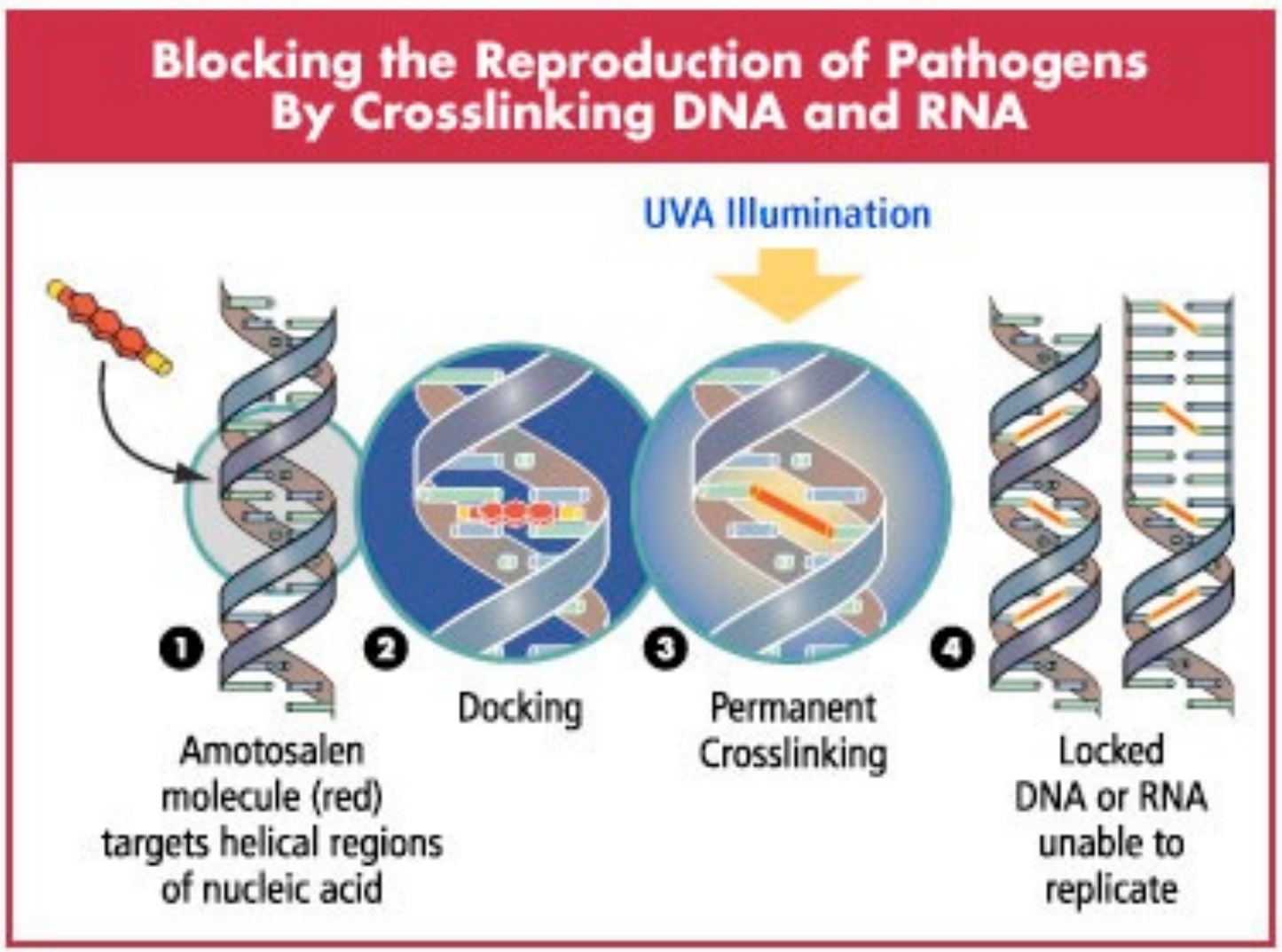
SwissTransfusion 2012, September 6th

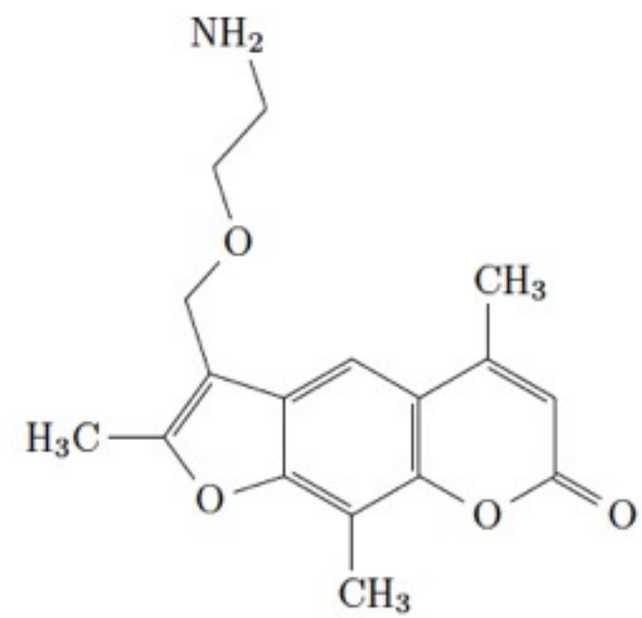
Outline

- The Intercept process for plasma
- Incentive for introducing Intercept in Lausanne
- Quality of Intercept-treated plasmas
- Project status

The Intercept process

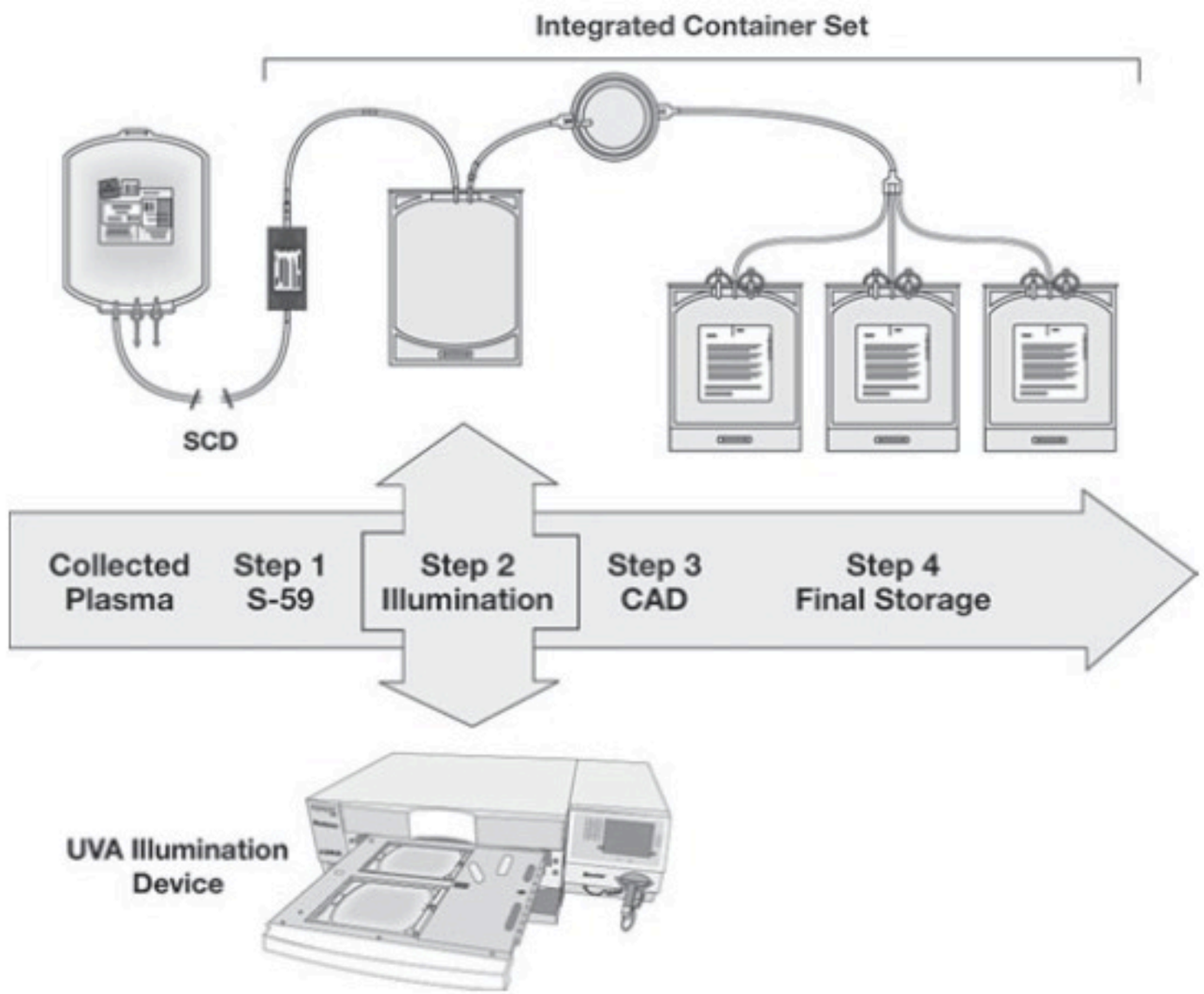
Process very similar to platelets





Amotosalen

Illumination and CAD



The Intercept guardbands

	Min	Max
Volume (including anticoagulant)	385 mL	650 mL
Red blood cells		4.10^9 /L

The Intercept process

- Final product: 200 ± 20 mL
- In-process loss: 30 mL
- 385 mL < Vol < 430 mL: 1 final bag
- 430 mL < Vol < 630 mL: 2 final bags
- 630 mL < Vol < 650 mL: 3 final bags

Complete freezing within 20 hours post-donation.

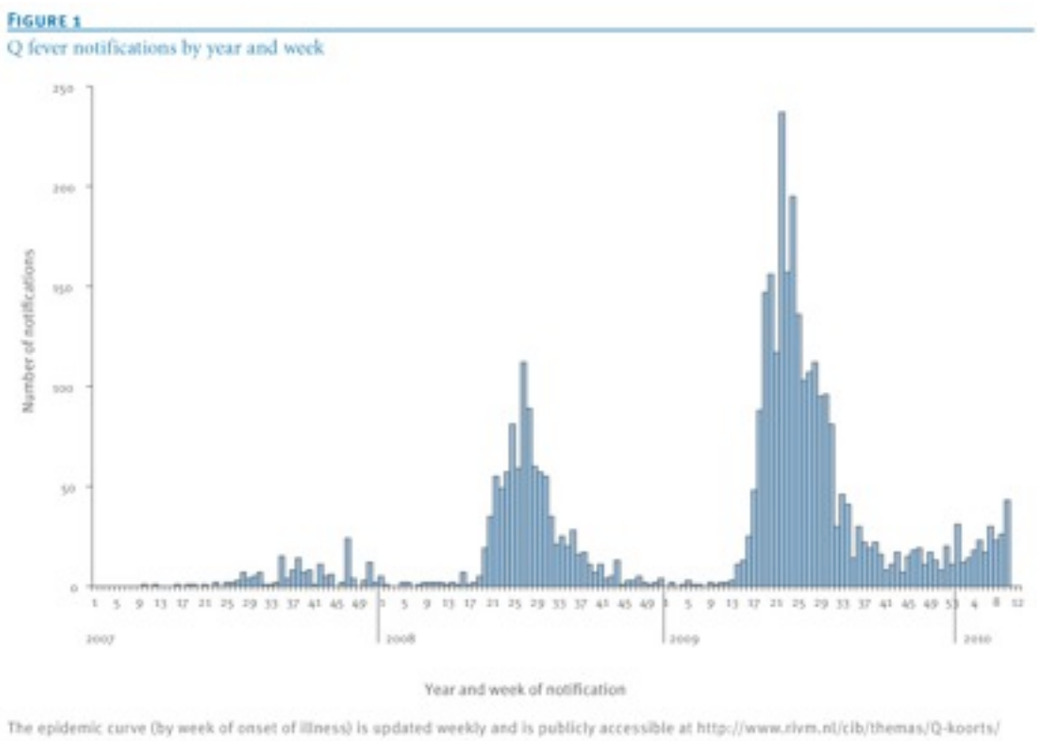
Incentive for the introduction of Intercept

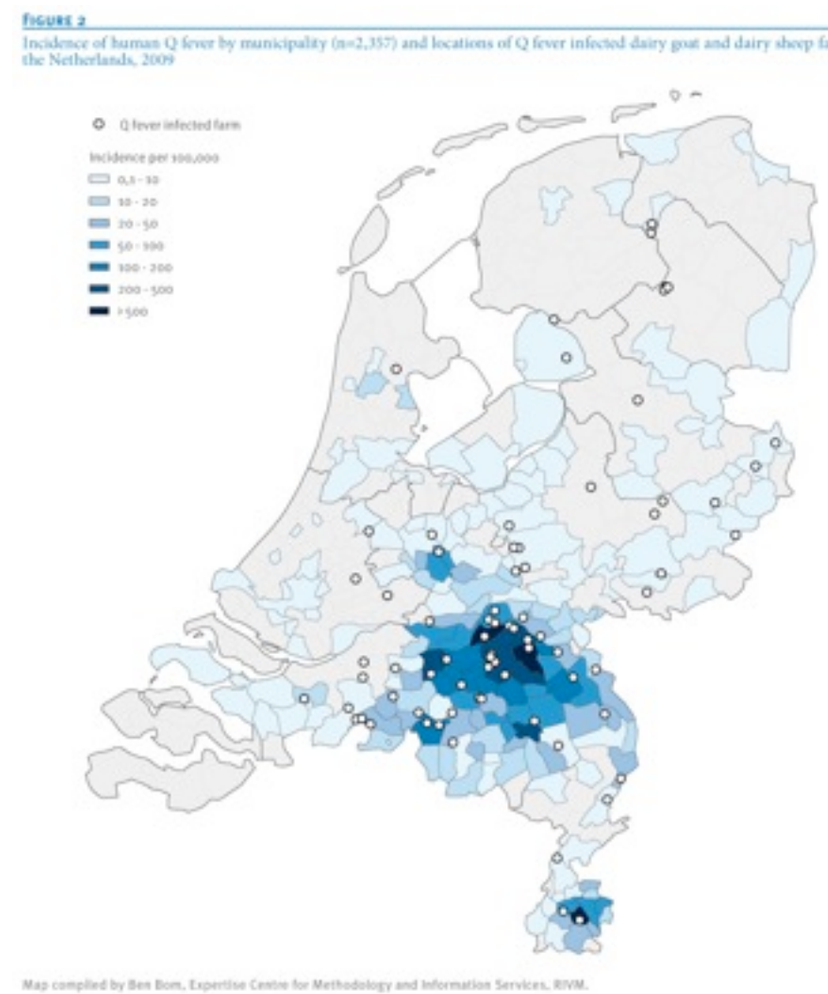
- Currently in Lausanne, we buy external quarantine plasma for transfusion
- We seek a valorization of our plasmas in the context of high pressure on fractionation plasma prices
- PI may represent a logistically simpler way of producing transfusion plasma
- Quarantine plasma is considered as safe against HIV, HBV, HCV, but....

Emerging diseases

- Episodes of Q fever in Wallis in 1983, in Vaud in 2012 (14 cases, no donor)

- Recurrent epidemies of Q fever in the Netherlands





Eurosurveillance, Volume 15, Issue 12, 25 March 2010

West Nile Virus in Italy (2009)

Hundreds of horses have been affected (25% deaths)

Other places, other pathogens...

Transboundary and Emerging Diseases

Transboundary and Emerging Diseases

ORIGINAL ARTICLE

Monitoring of the West Nile Virus epidemic in Spain between 2010 and 2011

I. García-Bocanegra[1], J. A. Jaén-Téllez[2], S. Napp[3], A. Arenas-Montes[1], M. Fernández-Morente[2], V. Fernández-Molera[2] and A. Arenas[1]

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[2] Consejería de Agricultura y Pesca de la Junta de Andalucía, Sevilla, Spain
[3] Centre de Recerca en Sanitat Animal (CReSA), UAB-IRTA, Campus de la Universitat Autònoma de Barcelona, Barcelona, Spain

RAPID COMMUNICATIONS

First two autochthonous dengue virus infections in metropolitan France, September 2010

G La Ruche (g.laruche@invs.sante.fr)[1], Y Souarès[1], A Armengaud[2], F Peloux-Petiot[3], P Delaunay[4], P Desprès[5], A Lenglet[6], F Jourdain[7], I Leparc-Goffart[8], F Charlet[3], L Ollier[4], K Mantey[6], T Mollet[6], J P Fournier[4], R Torrents[2], K Leitmeyer[6], P Hilairet[4], H Zeller[6], W Van Bortel[6], D Dejour-Salamanca[1], M Grandadam[5], M Gastellu-Etchegorry[1]

1. French Institute for Public Health Surveillance (Institut de Veille Sanitaire, InVS), Saint-Maurice, France
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3. Regional Health Agency of Provence-Alpes-Côte d'Azur, Marseille and Nice, France
4. Entomology-Parasitology, Virology and Emergency Medicine and Internal Medicine Departments, University Hospital of Nice, Nice, France
5. Institut Pasteur, National Reference Centre for arboviruses, Paris, France
6. European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden
7. Directorate General for Health, Ministry of Health, Paris, France
8. Institut de recherche biomédicale des armées, National Reference Centre for arboviruses associated laboratory, Marseille, France

Chikungunya in Italy

Eurosurveillance, Volume 12, Issue 36, 06 September 2007

Articles

Citation style for this article: Angelini R, Finarelli AC, Angelini P, Po C, Petropulacos K, Macini P, Fiorentini C, Fortuna C, Venturi G, Romi R, Majori G, Nicoletti L, Rezza G, Cassone A. An outbreak of chikungunya fever in the province of Ravenna, Italy. Euro Surveill. 2007;12(36):pii=3260. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=3260

An outbreak of chikungunya fever in the province of Ravenna, Italy

R Angelini[1] AC Finarelli[2], P Angelini[2], C Po[2], K Petropulacos[3], P Macini[2], C Fiorentini[4], C Fortuna[4], G Venturi[4], R Romi[4], G Majori[4], L Nicoletti[4], G Rezza[4], A Cassone (cassone@iss.it)[4]

1. Dipartimento Sanità Pubblica, Azienda Unità Sanitaria Locale (Department of Public Health, Local Health Unit), Ravenna, Italy
2. Servizio di Sanità Pubblica, Regione Emilia-Romagna, Bologna, Italy
3. Servizio Presidi ospedalieri, Regione Emilia-Romagna, Bologna, Italy
4. Department of Infectious, Parasitic and Immunomediated Diseases, Istituto Superiore di Sanità, Rome, Italy

Vector colonization

Medical and Veterinary Entomology (2009) **23**, 448–451

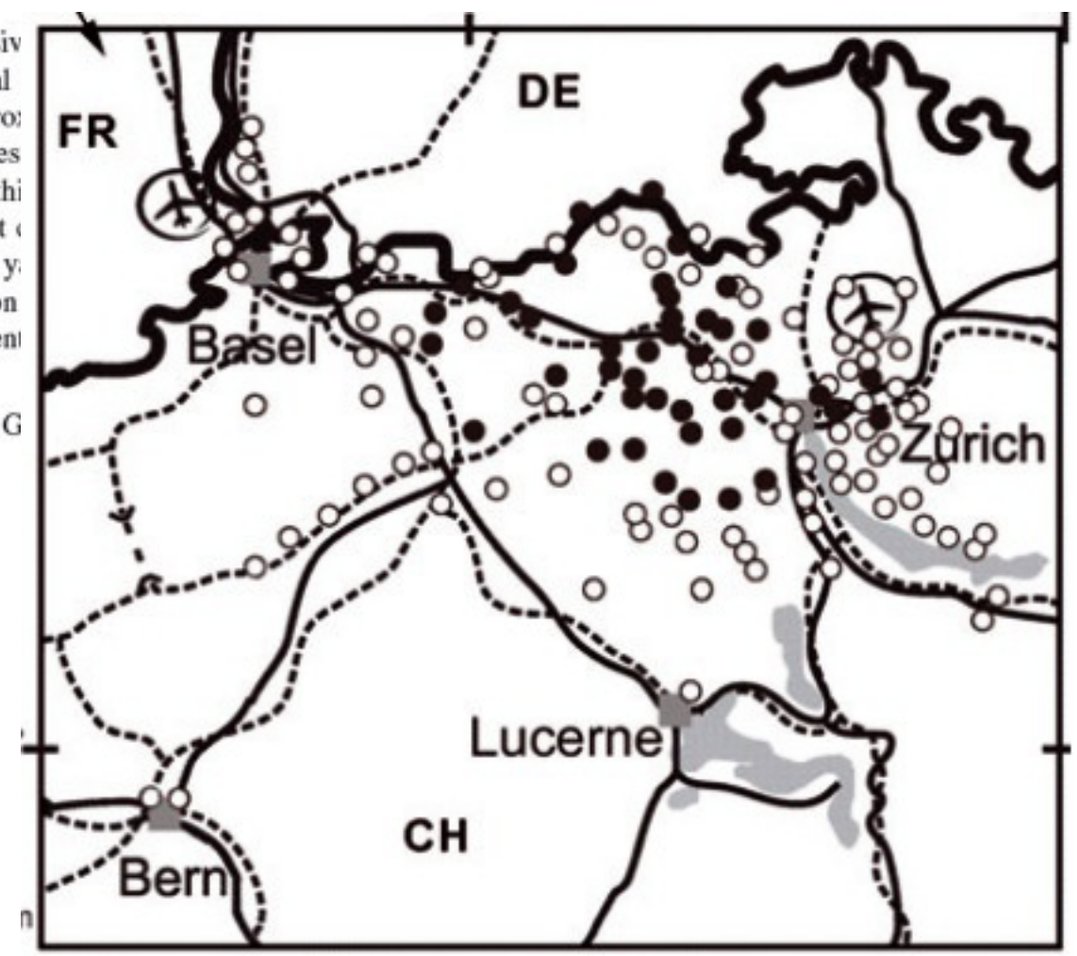
SHORT COMMUNICATION

The invasive mosquito *Aedes japonicus* in Central Europe

F. SCHAFFNER, C. KAUFMANN, D. HEGGLIN and A. MATHIS
Institute of Parasitology, Swiss Reference Laboratory for Vector Entomology, University of Zurich, Zurich, Switzerland

Abstract. Complaints about a biting pest led to the recognition of invasiv
(Finlaya) japonicus japonicus (Theobald) (Diptera: Culicidae) in Central
Larval collections from cemetery vases revealed a colonized area of appro
1400 km^2 in northern Switzerland spreading into bordering Germany, sugges
the mosquito has been established in this region for several years. Within thi
larvae of *Ae. japonicus* were recovered from more containers than the most
resident culicid species *Culex pipiens*. Possible introduction sites (used tyre y
international airports) revealed few or no larvae, and the mode of introduction
unclear. Given the vector potential of this species for arboviruses, implemen
surveillance and control measures should be considered.

Key words. *Aedes*, Culicidae, larva, invasion, vector, Europe, Switzerland, G



Aedes Japonicus is a vector for yellow fever and encephalitis

Efficiency of the Intercept process - viruses

Viruses Tested Using the INTERCEPT Blood System	Extent of Inactivation* (log_{10} reduction)	
	Platelets in plasma/Additive solution	Platelets in plasma
Enveloped Viruses		
HIV-1 (cell-associated)***	>6.1	>6.7
HIV-1 (cell-free)	>6.2	≥4.7
Clinical isolate of HIV-1	>3.4	-
Clinical isolate of HIV-2	>2.5	-
Latent proviral HIV-1	Inactivated to the limit of detection	-
HBV (strain MS-2)	>5.5	>4.5
HCV (strain Hutchison)	>4.5	>4.5
HTLV-I (Human T-cell Lymphotropic Virus)***	4.7**	≥4.5
HTLV-II (Human T-cell Lymphotropic Virus)***	5.1**	>5.7
Cell-associated Cytomegalovirus (CMV)***	>5.9	-
Bovine Viral Diarrhea Virus (BVDV, model virus for human HCV)	>6.0	≥5.4
Duck Hepatitis B Virus (DHBV, model virus for human HBV)	>6.2	4.4 to 4.5
PRV (Pseudorabies virus, model for CMV)	-	≥4.7
West Nile virus	>6.0	≥6.8
SARS-CoV (Human Corona virus)	-	≥5.5
Chikungunya virus	>6.4	≥7.6
Influenza A H5N1 virus (Avian Influenza)	>5.9	>5.7
Non-Enveloped Viruses		
Bluetongue Virus, type 11	>5.0	5.1
Calicivirus	1.7 to 2.4	-
Human Adenovirus-5	>5.9	≥6.9
Parvo (Parvovirus B19)	-	1.8

Viruses Tested Using the INTERCEPT Blood System for Plasma	Extent of Inactivation* (log_{10} reduction)
Enveloped Viruses	
HIV-1 (cell-associated)**	>6.7
HIV-1 (cell-free)	>6.8
HBV (strain MS-2)	>4.5
HCV (strain Hutchison)	>4.5
HTLV-I (Human T-cell Lymphotropic Virus)**	≥4.5
HTLV-II (Human T-cell Lymphotropic Virus)**	>5.7
WNV (West Nile Virus)	≥6.8
SARS-CoV (Human Corona Virus)	≥5.5
BVDV (Bovine Viral Diarrhea Virus, model virus for human HCV)	≥6.0
DHBV (Duck Hepatitis B Virus, model virus for human HBV)	4.4 - 4.5
Chikunguyna virus	≥7.6
Influenza A H5N1 virus (Avian Influenza)	>5.7
Non-Enveloped Viruses	
BTV (Bluetongue Virus)	5.1
Human Adenovirus-5	≥6.9
Parvo (Parvovirus B19)	1.8

Efficiency of the Intercept process - bacteria

Bacterial Species Tested Using the INTERCEPT Blood System	Extent of Inactivation* (log_{10} reduction)	
	Platelets in plasma/Additive Solution	Platelets in plasma
Gram-Negative Bacteria		
Escherichia coli	>6.4	≥7.3
Serratia marcescens	>6.7	-
Klebsiella pneumoniae	>5.6	≥6.7
Pseudomonas aeruginosa	4.5	-
Salmonella choleraesuis	>6.2	-
Yersinia enterocolitica	>5.9	>7.3
Enterobacter cloacae	5.9	-
Anaplasma phagocytophilum (HGE agent)**	-	>4.2
Gram-Positive Bacteria		
Staphylococcus epidermidis	>6.6	>7.4
Staphylococcus aureus	6.6	>7.6
Streptococcus pyogenes	>6.8	-
Listeria monocytogenes	>6.3	-
Corynebacterium minutissimum	>6.3	-
Bacillus cereus (includes spores)	3.6	-
Bacillus cereus (vegetative)	>6.0	-
Bifidobacterium adolescentis	>6.5	-
Propionibacterium acnes	>6.7	-
Lactobacillus species	>6.9	-
Clostridium perfringens (vegetative form)	>7.0	-
Spirochete Bacteria		
Treponema pallidum (syphilis)	≥6.8 to ≤7.0	>5.9
Borrelia burgdorferi (Lyme disease)	>6.8	>10.6

Bacterial Species Tested Using the INTERCEPT Blood System for Plasma	Extent of Inactivation* (log_{10} reduction)
Gram-Negative Bacteria	
Klebsiella pneumoniae	≥7.4
Yersinia enterocolitica	>7.3
Anaplasma phagocytophilum (HGE agent)	>4.2
Gram-Positive Bacteria	
Staphylococcus epidermidis	>7.3
Spirochete Bacteria	
Treponema pallidum (syphilis) **	>5.9
Borrelia burgdorferi (Lyme disease)	>10.6

Efficiency of the Intercept process - parasites

Parasites Tested Using the INTERCEPT Blood System	Extent of Inactivation* (log10 reduction)	
	Platelets in plasma/Additive Solution	Platelets in plasma
*Plasmodium falciparum*** (malaria)	≥6.0	≥6.9
Trypanosoma cruzi (Chagas' disease)	>5.3	>5.0
Leishmania mexicana (metacyclic promastigote stage)	>5.0	-
Leishmania major Jish (amastigote stage)	>4.3	-
Babesia microti (babesiosis)	>5.3	>5.3

Parasites Tested Using the INTERCEPT Blood System for Plasma	Extent of Inactivation* (log_{10} reduction)
*Plasmodium falciparum*** (malaria)	≥6.9
Trypanosoma cruzi (Chagas' disease)	>5.0
Babesia microti (babesiosis)	>5.3

Quality of Intercept-treated plasmas

In vitro coagulation studies

- Validation study performed in three centers (Strasbourg, Lübeck and Bergen) on pooled whole blood plasmas and plasmapheresis plasmas
- Plasmas were treated and frozen within eight hours
- All coagulation studies were performed in one site

Schlenke et al, Transfusion 2008;48:697-705

Parameter	Reference range	Control	Intercept	Retention
PT (sec)	11.1-13.5	11.8±0.6	12.2±0.6	0.4±0.2
aPTT (sec)	23-35	28.0±2.3	32.1±3.2	4.1±1.2
FI (mg/dL)	200-390	291±49	217±43	74±6
FII (IU/dL)	80-120	105±13	93±13	89±4
FV (IU/dL)	95-170	126±22	122±20	97±3
FVII (IU/dL)	70-175	112±21	90±17	81±3
FVIII (IU/dL)	85-235	131±34	97±29	74±5
FIX (IU/dL)	75-145	94±13	79±11	84±4
FX (IU/dL)	75-130	109±15	96±14	88±3
FXI (IU/dL)	60-150	97±17	84±17	86±6
FXIII (IU/dL)	85-135	116±18	110±17	95±5
PC (IU/dL)	80-140	118±20	101±18	86±6
PS (IU/dL)	85-135	109±20	105±19	97±5
AT (IU/dL)	85-105	98±9	94±9	96±3
AP (IU/dL)	80-150	99±11	82±7	83±6

Schlenke et al, Transfusion 2008;48:697-705

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Factor retention at 20 hours, thawed plasma

In-put Plasma	Before IBS FVIII (IU/dL)	After IBS FVIII (IU/dL)	Retention of FVIII (%)
Apheresis, 8 hour (n=90)	141 ±41	107 ±35	75 ±6
Apheresis, 8 hour, previously frozen (n=55)	128 ±41	96 ±31	75 ±4
WB-derived, 8 hour (n=96)	121 ±23	88 ±18	73 ±5
WB-derived, 20 hour (n=32)	97 ±18	69 ±13	71 ±4

*Pinkoski L, Corash L. Vox Sang 2009;96 (suppl.1):231-232

- Factor VIII activity is retained as well when treatment and freezing is performed within 20 hours post-collection
- Factor VIII ≥ 50 IU/dL
- Retention ≥ 70%

Status of the project

National validation plan

- Validation plan elaborated in collaboration with Edith Goossenaerts (Cerus), David Goslings (BSD Zurich)
- Submitted to Swissmedic in early June 2012
- Questions from Swissmedic in July 2012
- Revision to be submitted next week
- Request for modification to be filed by Cerus (pooling of apheresis plasma, guardband on leukocytes)

Validation plan

- Very similar to platelets: one national validation plan with two (?) pilot centers

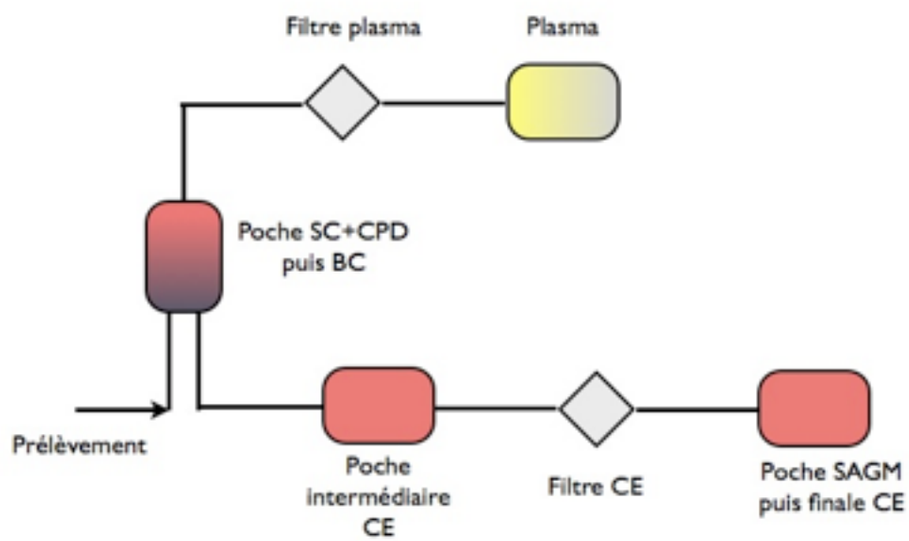
- Pre-validation: preparation of 12 units of plasma ready for Intercept to demonstrate the compliance to guardbands (volume, RBC) and establish baseline values for Fibrinogen and Factor VIII.

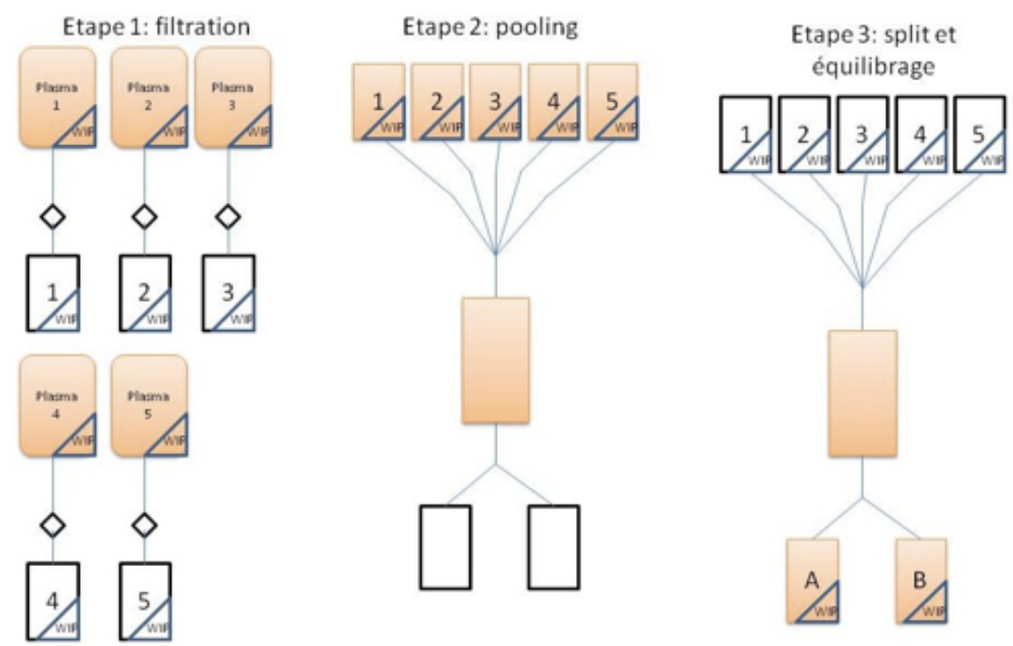
- Validation: 12 Intercept processes with same type of plasma, to check that the process is under control (retention of Fibrinogen and Factor VIII, amotosalen residual levels) and compliance to Swiss regulations for final units (Factor VIII absolute values, leukocyte contaminations)

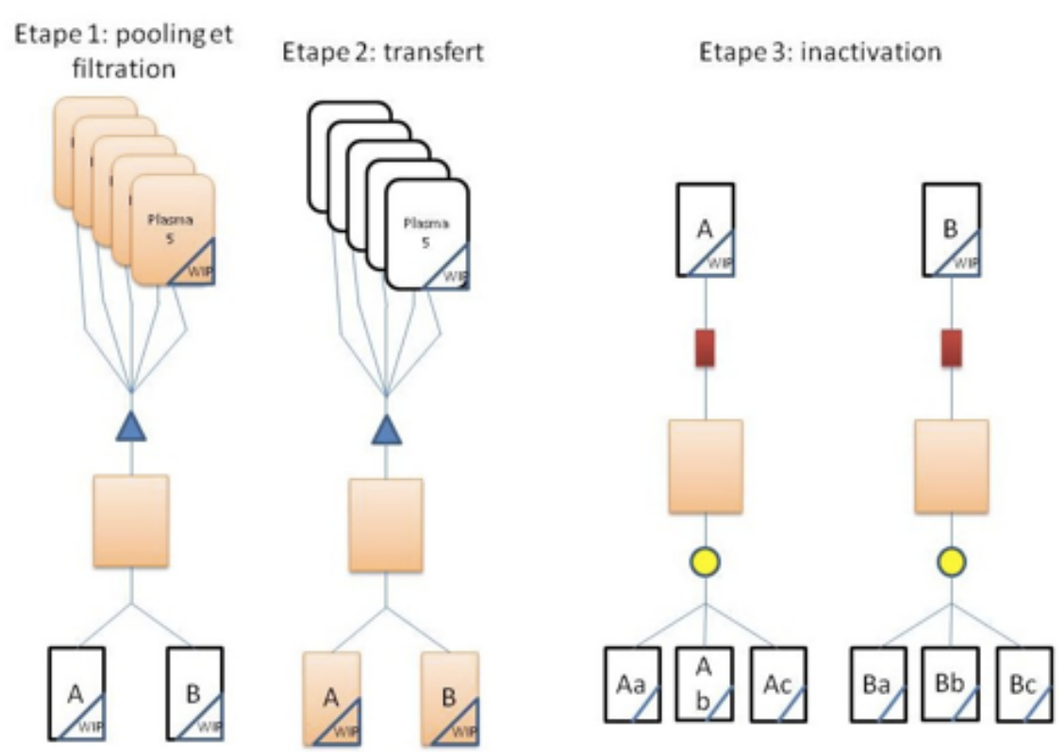
To be done before routine

- Implementation / adaptation of plasmapheresis
- Development of a whole-blood process (pooling of 2-6 leukocyte-reduced plasmas)
- IT aspects (product codes, pooling, product transformations)
- operational implementation

Whole blood plasmas - various schemes possibles







Pooling number game

- Pools of 2-6 plasmas are filtered (losses of 17 mL per pool)
- In-process losses of 30 mL during Intercept

Number of plasmas (260 mL)	Post-filtration pooled volume (mL)	Intercept kits | losses (mL)	Final volume (mL) | Number of plasmas | Excedance (mL)
2	503	1 | 0 mL	473 mL | 2 | 73 mL
3	763	1 | 113 mL	620 mL | 3 | 20 mL
4	1023	2 | 0 mL	962 mL | 4 | 162 mL
5	1283	2 | 0 mL	1223 mL | 6 | 23 mL
6	1543	2 | 243 mL	1240 mL | 6 | 40 mL

Planning

Intercept validation may be done in October-November 2012, but routine will not start before early 2013....

Thanks

- David Goslings (BSD Zurich)
- Thomas Schulzki (T-CH, LPNM)
- Behrouz Mansouri (T-CH)
- Edith Goossenaerts, Marc Slaedts (Cerus)

Thank you for your attention