

Photochemical Inactivation of Chikungunya Virus in Human Apheresis Platelet Components by Amotosalen and UVA Light

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Abstract. Chikungunya virus (CHIKV) is a mosquito-borne alphavirus that recently re-emerged in Africa and rapidly spread into countries of the Indian Ocean basin and South-East Asia. The mean viremic blood donation risk for CHIKV on La Réunion reached 1.5% at the height of the 2005–2006 outbreaks, highlighting the need for development of safety measures to prevent transfusion-transmitted infections. We describe successful inactivation of CHIKV in human platelets and plasma using photochemical treatment with amotosalen and long wavelength UVA illumination. Platelet components in additive solution and plasma units were inoculated with two different strains of high titer CHIKV stock (6.0–8.0 logs/mL), and then treated with amotosalen and exposure to 1.0–3.0 J/cm² UVA. Based on *in vitro* assays of infectious virus pre- and post-treatment to identify endpoint dilutions where virus was not detectable, mean viral titers could effectively be reduced by $> 6.4 \pm 0.6 \log_{10}$ TCID₅₀/mL in platelets and $\geq 7.6 \pm 1.4$ logs in plasma, indicating this treatment has the capacity to prevent CHIKV transmission in human blood components collected from infected donors in or traveling from areas of CHIKV transmission.

INTRODUCTION

Emergence/re-emergence of arthropod-borne viruses (arboviruses) in new geographic ranges poses a considerable challenge for transfusion medicine worldwide. Highlighted by the West Nile virus (WNV) epidemics in North America, dengue virus (DENV) epidemics in Puerto Rico, Brazil, and Honduras, and the establishment of DENV transmissions in Florida, arboviruses are now considered as “significant transfusion-transmissible pathogens.”¹ The 2012 WNV data for the United States include over 240 presumptive viremic blood donors—already exceeding the total of 137 for 2011²; although both WNV and DENV are members of the *Flaviviridae*, chikungunya virus (CHIKV) is in the *Alphavirus* genus of the family *Togaviridae*. Beginning in 2004, an epidemic of CHIKV emerged in coastal areas of East Africa^{3,4} and rapidly spread into countries of the Indian Ocean basin,^{5–9} South-East Asia,^{10–13} India,¹⁴ China,¹⁵ and Europe.^{16–18} The total number of CHIKV infections remains undetermined, although in India alone it has been estimated that it has recently caused between 2 and 6.5 million cases of arthritic disease.¹⁹ In addition, fatalities were repeatedly documented in association with CHIKV infection, although involvement of underlying medical conditions or coinfections with other pathogens in fatal cases could not be disregarded.^{20–25} There are no antivirals or licensed vaccines available to control CHIKV outbreaks.

Enzootic in tropical regions of Africa, CHIKV relies on transmission between non-human primates and sylvatic, primateophilic mosquitoes (*Aedes furcifer-taylori*, *Aedes africanus*, *Aedes luteocephalus*, and *Aedes neoaffricanus*).^{26,27} Occasional spillovers result in CHIKV introduction into rural areas causing outbreaks transmitted by highly anthropophilic *Aedes aegypti* and *Aedes albopictus* mosquitoes. The CHIKV is also endemic in South-East Asia where it is maintained in a strictly urban cycle involving *Ae. aegypti* and most recently,

Ae. albopictus.²⁶ The genetic adaptation of CHIKV to transmission by *Ae. albopictus* was postulated as one of the major factors that contributed to the magnitude and geographic dispersal of the recent CHIKV epidemics.^{28,29} *Aedes albopictus* is now present on all continents except Antarctica and continues to expand its range,³⁰ posing the threat of introduction and possible establishment of CHIKV in new geographic areas including the Americas. The CHIKV outbreaks in Northern Italy in 2007 and France in 2010^{16–18} underscore the plausibility of future expansion of CHIKV.

Although CHIKV infection by transfusion of donated blood products has not been documented, the explosive global CHIKV expansion in recent years warrants a considerable revision of blood management systems in affected regions.¹ Thus, during the Italian CHIKV outbreak of 2007 and the 2005–2006 epidemic in the French island La Réunion, all blood collections were suspended,^{31–33} and the required blood was delivered from unaffected regions of Italy or continental France. However, the 5-day shelf life of platelet components precluded their being delivered to La Réunion from France and pathogen inactivation was instituted on an emergency basis to provide safe platelets for patients there.³² The relatively short duration of the viremic period (6–7 days) and low rates of asymptomatic infections (3% to 25%)^{34–36} have been proposed as factors that decrease the risk of contamination of donated blood with CHIKV.¹ However, the extremely high attack rates observed during CHIKV epidemics (34–75%) probably equalize these factors, resulting in an overall increase in the transfusion risk of CHIKV.^{3,5,37} Using mathematical models, it was estimated that during the 2005–2006 outbreak in La Réunion, the mean viremic blood donation risk was 0.132% and reached 1.5% at the height of the outbreak.³³ Analysis of donated platelets for the presence of CHIKV RNA in Italy revealed a 0.4% contamination rate, which is in agreement with the mathematical model prediction (0.7%).³¹

The photochemical treatment of therapeutic units of human platelet and plasma components using amotosalen, a synthetic psoralen, and UVA (320–400 nm; INTERCEPT Blood System [IBS]; Cerus Corporation, Concord, CA) is a highly efficient method for inactivation of a broad variety of blood borne pathogens, including bacteria, viruses, protozoa, and leukocytes.^{38–46}

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The inactivation technology is based on the ability of psoralens to intercalate into double-stranded forms of RNA or DNA, or hairpins of single-stranded RNA or DNA. Treatment of the resultant complexes with UVA illumination leads to the formation of inter- and cross-strand links between pyrimidine bases, which prevents pathogen replication and transcription.⁴⁷ *In vitro* studies have shown that photochemical treatment with amotosalen and UVA does not substantially affect platelet or plasma function^{40,41,48,49} and clinical trials indicated that transfusion of psoralen-treated platelets or plasma to patients does not result in adverse immunologic or hemorrhagic responses.^{50–53} More than a million kits to prepare IBS platelets and plasma have been sold since the introduction of the system in Europe. Detailed haemovigilance and post marketing surveillance in Europe since 2003 continues to demonstrate safety and efficacy of the treated products.^{54–58}

Although high levels of inactivation have been demonstrated for a number of viruses including single-stranded RNA viruses,^{38,40} the efficacy of amotosalen and UVA treatment of inactivation of high CHIKV doses had not been tested. Here, we describe the successful inactivation of high doses of CHIKV in apheresis platelet concentrates and plasma components using the amotosalen and UVA treatment process.

MATERIALS AND METHODS

CHIKV strain LR2006 OPY1 (GenBank accession no.: DQ443544.2), was obtained from the World Reference Center for Emerging Viruses and Arboviruses (WRCEVA) at the University of Texas Medical Branch, Galveston, TX. The strain was originally isolated in 2006 from a febrile patient who returned to France from La Réunion. The strain was passed five times on Vero cell culture and once in suckling mice. The stock virus was prepared by infecting confluent monolayers of Vero76 cells (obtained from ATCC, Rockville, MD) in 150 cm² flasks. Virus was propagated in Vero cells at 37°C in Liebovitz's L-15 medium (1X L-15, 10% fetal bovine serum, 10% tryptose phosphate broth, 100 U/mL penicillin, and 100 µg/mL streptomycin, 2 mM L-Glutamine), harvested at 3 days post infection, aliquoted, and stored at –80°C. The CHIKV strain S27 was obtained from the ATCC and was propagated in Vero76 cells as described previously, using Earle's Minimal Essential Medium (EE) in place of L-15. This strain was originally isolated from patient serum in Tanganyika, East Africa in 1953. The use of two different strains isolated decades apart shows that viruses containing different mutations accumulated over time are equally sensitive to the inactivation protocol presented here.

Apheresis platelet concentrates, collected with the Amicus cell separator (Fenwal Inc., Lake Zurich, IL) from randomly selected routine donors, were suspended in ~110 mL autologous plasma and 180 mL of InterSol platelet additive solution (NaAcetate·3H₂O, 4.42 g/L; Na₃Citrate·2 H₂O, 3.18 g/L; NaH₂PO₄·2H₂O, 1.05 g/L; Na₂HPO₄, 3.05 g/L; NaCl, 4.52 g/L, Fenwal Inc.). Each platelet concentrate was collected in acid citrate dextrose anticoagulant according to AABB (formerly the "American Association of Blood Banks") standards to contain ~2.8 × 10¹¹ to 4.2 × 10¹¹ platelets per unit. Platelets were supplied by The Memorial Blood Center (St. Paul, MN). Plasma components were collected in sodium citrate anticoagulant on the Haemonetics PCS (Haemonetics Corp., Braintree, MA) and were obtained as fresh-frozen plasma from Plasma Biological Services (Memphis, TN).

Four replicate experiments were performed in platelet and plasma components. For each replicate two ABO-matched platelet units or two thawed, fresh-frozen plasma units were pooled. The volume of each platelet pool was adjusted to ~610 mL, as determined by weight (density is 1.01 g/mL), with 37% autologous plasma/63% InterSol. The volume of each plasma pool was adjusted to ~1,200 mL (density 1.023 g/mL). Approximately 30 mL was removed from each pool and set aside. An aliquot of a previously prepared frozen stock of CHIKV was quickly thawed in a 37°C water bath and 0.5 mL was collected for titer determination. Six mL of CHIKV stock was added to the platelet pool by a Luer lock and 13 mL was added to the plasma pool, resulting in a titer of ~10⁶ and 10⁸ 50% tissue culture infectious doses (TCID₅₀)/mL, respectively. The previously withdrawn 30 mL of blood component was then returned to the appropriate container through the same Luer lock, rinsing any residual virus through the docking tube and into the container. After mixing, each pool was split into two units, generating a unit 1 and unit 2 for each experimental replicate. Each platelet unit was ~285 mL and each plasma unit ~585 mL.

Each platelet and plasma unit was sterilely connected to the appropriate INTERCEPT processing set (Cerus Corporation) and the contents were passed through a PL 2411 plastic container holding 15 mL of 3 mM (platelets) or 6 mM (plasma) amotosalen, and into a PL 2410 plastic illumination container, resulting in a final amotosalen concentration of ~150 µM. Samples were collected to determine the initial virus titer.

Each unit 1 received a single 3.0 J/cm² UVA treatment, and each unit 2 received two consecutive 1.03 J/cm² treatments. These doses are equal to or less than the treatment doses used commercially. Illumination was performed using an INTERCEPT illuminator (INT100, Cerus Corporation) according to the instrument manual. The single 3.0 J/cm² UVA treatment reflects the commercial INTERCEPT process, whereas the 1.0 and 2.1 cm² UVA treatments were used to demonstrate inactivation kinetics. Following each illumination (single 1.0 J/cm², cumulative 2.1 J/cm², and single 3.0 J/cm²), samples were withdrawn for CHIKV titer determination. All samples were frozen at –80°C until assayed.

To assess and quantify CHIKV viability, pre-illumination and stock virus samples were 10-fold serially diluted in L-15 medium with 5 U/mL heparin (platelet samples) or EE medium with 5 U/mL heparin (plasma samples). Heparin was included in the diluents to prevent the formation of clots when the anticoagulant in the blood product comes in contact with the divalent cations in the culture medium. Clots are disruptive to the cells and may cause a loss of assay sensitivity. Post-illumination samples were diluted 1:5 (platelets) or 1:4 (plasma), 1:10, and 1:100 in the same diluents. For platelet samples, 100 µL of each 1:10 and 1:100 dilution were added to 8 wells of a 96-well plate and 100 µL of each 1:5 dilution was added to 240 wells. One hundred µL of L-15 growth medium with 5 U/mL heparin containing ~5 × 10⁵ cells/mL of Vero cells were added to each well of the plate and plates were incubated at 37°C for 7 days before fixing and staining with a fixative containing amido black. The plates were then scored manually for infection by evaluating the cell monolayer for cytopathic effect. For plasma samples, 100 µL of each dilution of the pre-illumination samples was added to each of 6 wells of a 96-well plate containing Vero76 cells.

TABLE 1

Chikungunya virus (strain OPY1) inactivation in platelet concentrates after photochemical treatment with 150 μ M amotosalen and varying UVA treatments

Replicate	Titer ($\text{Log}_{10}\text{TCID}_{50}/\text{mL}$)					Log reduction*		
	Unit 1		Unit 2			Unit 1	Unit 2	
	Pre-UVA	Post 3.0 J/cm ²	Pre-UVA	Post 1.0 J/cm ²	Post 2.1 J/cm ²	3.0 J/cm ²	1.0 J/cm ²	2.1 J/cm ²
1	4.8	< -0.7	4.6	< -0.7	< -0.7	> 5.5	> 5.2	> 5.2
2	6.1	< -0.7	5.8	< -0.7	< -0.7	> 6.7	> 6.5	> 6.5
3	6.1	< -0.7	5.9	< -0.7	< -0.7	> 6.7	> 6.6	> 6.6
4	6.1	< -0.7	5.7	< -0.7	< -0.7	> 6.7	> 6.3	> 6.3
Mean \pm SD†	5.7 \pm 0.6	< -0.7	5.5 \pm 0.6	< -0.7	< -0.7	> 6.4 \pm 0.6	> 6.2 \pm 0.6	> 6.2 \pm 0.6

*Log reduction was calculated as $\log(\text{pre-UVA titer} \div \text{post-UVA titer})$ where titers are expressed as $\text{Log}_{10}\text{TCID}_{50}/\text{mL}$. Log reduction was calculated from numbers that were not rounded. Means and standard deviations (SD) were determined from numbers that were not rounded.

The 1:4 dilution of each post-illumination plasma sample was added to 216 wells (unit 1) or 72 wells (unit 2), and the 1:10 and 1:100 dilutions of all post-illumination plasma samples were added to 12 wells of a 96-well plate containing Vero76 cells. The plates were incubated at 37°C in a humidified CO₂ atmosphere and the cytopathic effect was evaluated using a light microscope every 1–2 days starting on Day 3 and continuing through Day 7 or 8. Each well was scored as positive or negative for cytopathic effect. Following scoring, a titer was calculated for each sample using the method of Reed and Muench⁵⁹ based on the number of positive and negative wells in each dilution. For samples in which no viable CHIKV was detected in any of the wells inoculated (post-UVA samples), the titer was calculated as less than what the titer would be if one infectious virion were present in the total volume of blood product assayed. A large number of wells were inoculated with the 1:4 and 1:5 dilutions to maximize the total amount of treated blood product evaluated and thus to maximize the dynamic range of the assay and the level of inactivation demonstrated. Mean titers and SD for four replicates were expressed as $\text{TCID}_{50}/\text{mL}$ of sample.

RESULTS

To evaluate CHIKV inactivation in human apheresis platelet concentrates and plasma components by photochemical treatment with amotosalen (150 μ M) and UVA, CHIKV was added to platelet concentrates to titers of $\sim 6 \text{ Log}_{10}\text{TCID}_{50}/\text{mL}$ (strain OPY1) and to plasma components to a titer of $\sim 8 \text{ Log}_{10}\text{TCID}_{50}/\text{mL}$ (strain S27). The two titers used represent the highest titers attainable for each strain tested. Vanlandingham

and others⁶⁰ recently published the molecular characterization of the OPY1 strain of CHIKV using a reverse transcription-polymerase chain reaction assay and have correlated the infectivity with the genomic equivalents per mL (gEq/mL). A 200:1 relationship was found indicating that the molecular titer in platelets was $\sim 8 \text{ log gEq/mL}$. If the ratio of gEq to infectious titer is similar for the S27 strain as expected, molecular titers of $\sim 10 \text{ log gEq/mL}$ were achieved in plasma since the starting titer of CHIKV S27 was higher. The components were then treated with amotosalen and 3.0, 2.1, or 1.0 J/cm² UVA. The CHIKV was completely inactivated to the limit of detection ($< -0.7 \text{ Log}_{10}\text{TCID}_{50}/\text{mL}$) at all experimental conditions in platelet components, resulting in inactivation of $> 6.4 \pm 0.6 \text{ Log}_{10}\text{TCID}_{50}$ (Table 1). In plasma components, which were inoculated with 100-fold more CHIKV because of the higher stock virus titers achievable with strain S27, some residual viable virus was detected in some replicates of all experimental conditions (Table 2). However, inactivation to below the limit of detection in the assay was observed in half of the replicates following 3.0 J/cm² UVA treatment and fewer than 1.3 $\text{Log}_{10}\text{TCID}_{50}/\text{mL}$ was detected in the remaining replicates. Overall, inactivation of $\geq 7.6 \pm 1.4 \text{ log TCID}_{50}$ of CHIKV in plasma was observed (Table 2). Given the 200:1 ratio between the TCID_{50} and gEq/mL, levels of inactivation of > 8.7 and $> 9.9 \text{ log gEq}$ can be calculated for platelets and plasma, respectively, indicating a level of protection comparable to the highest levels of viremia observed in infected blood samples.^{61–63} Pre-illumination titers of CHIKV in both blood components were in the range of expected values based on the titer of the stock virus, indicating that neither amotosalen alone nor the blood products alone inactivated CHIKV, nor did the blood

TABLE 2

Chikungunya virus (strain S27) inactivation in plasma after photochemical treatment with 150 μ M amotosalen and varying UVA treatments

Replicate	Titer ($\text{Log}_{10}\text{TCID}_{50}/\text{mL}$)*					Log reduction†		
	Unit 1		Unit 2			Unit 1	Unit 2	
	Pre-UVA	Post 3.0 J/cm ²	Pre-UVA	Post 1.0 J/cm ²	Post 2.1 J/cm ²	3.0 J/cm ²	1.0 J/cm ²	2.1 J/cm ²
1	8.8	< -0.7	8.8	1.0 to 1.3	1.0 to 1.3	> 9.5	7.5 to 7.8	7.5 to 7.8
2	6.9	< -0.7	7.3	1.1 to 1.3	< -0.3	> 7.6	6.0 to 6.3	> 7.6
3	8.4	1.0 to 1.3	8.5	1.1 to 1.3	-0.3	7.1 to 7.4	7.2 to 7.4	8.8
4	7.5	1.0 to 1.3	7.5	1.1 to 1.3	1.0 to 1.3	6.2 to 6.5	6.1 to 6.4	6.2 to 6.4
Mean \pm SD‡	7.8 \pm 0.8	$\leq 0.3 \pm 1.2$	8.0 \pm 0.8	1.1 to 1.3	$\leq 0.4 \pm 0.7$	$\geq 7.6 \pm 1.4$	6.7 to 7.0	$\geq 7.5 \pm 1.1$

*Best and worst case titers were determined for samples in which at least one but less than half of the wells were positive in the most concentrated dilution plated (1:4). The worst case assumed that all the wells at the next lower dilution (undiluted) would have been positive if plated, and the best case assumed that 50% of the undiluted wells would have been positive if plated. Ranges in log reduction data are the result of using both best and worst case titers in log reduction calculations. When no virus was detected in the lowest dilution plated, the titer was determined to be < 1 in the total volume of blood product assayed.

†Log reduction was calculated as $\log(\text{pre-UVA titer} \div \text{post-UVA titer})$ where titers are expressed as $\text{Log}_{10}\text{TCID}_{50}/\text{mL}$. Log reduction was calculated from numbers that were not rounded.

‡Means and standard deviations (SD) were determined from numbers that were not rounded. Only worst case determinations were used in the calculations of means and SDs that were \geq or \leq the stated value.

products interfere with the sensitivity of detection of viable CHIKV (Tables 1 and 2).

DISCUSSION

Over the course of the last several years CHIKV has become one of the most important human pathogens in the alpha-virus family. The CHIKV epidemic, which started in coastal Kenya in 2004,⁴ rapidly spread into countries of South-East Asia, Indian Ocean basin,^{5–13} and India¹⁴ affecting millions of people. In addition, CHIKV was introduced into Europe where it caused its first autochthonous outbreaks in 2007 and 2010.^{16–18} Vectored by domestic *Ae. aegypti* and peridomestic *Ae. albopictus* mosquitoes widely distributed in the Old World and the Americas, CHIKV could potentially expand its range into the New World, where immunologically naive human populations could facilitate rapid spread of the virus. The consequences of such an event would have a considerable adverse effect on transfusion medicine.¹

In many regards, the potential impact of CHIKV on transfusion medicine is similar to that of WNV, except that assays for screening CHIKV in blood products, such as detection of CHIKV RNA, have not been developed and implemented, leaving deferral of donors based on travel history as the only option for reducing the CHIKV transfusion risk in non-endemic regions and no real options for risk reduction in endemic regions.¹ Although the majority of CHIKV infections are associated with febrile illness (> 75%)^{34,35} and these donors can be easily deferred, the viremic phase of CHIKV infections begins 1–2 days before the onset of symptoms, and about 6–20% of infections remain asymptomatic.³³ In addition, the extremely high attack rate during CHIKV outbreaks suggests that a considerable proportion of donated blood may be contaminated with CHIKV in epidemic areas.

In this study, we showed that photochemical treatment of human apheresis platelet and plasma components with amotosalen and UVA effectively inactivates high concentrations of CHIKV. In fact, the virus is sufficiently sensitive to this photochemical treatment that complete inactivation was achieved in platelet components with as little as one-third the UVA dose used in the commercial treatment process. In addition, the use of two different CHIKV strains, which were isolated several decades apart shows that the virus retains its sensitivity to inactivation, regardless of whatever mutations may have accumulated over that time. The robust inactivation achieved is particularly noteworthy in light of the fact that CHIKV is highly platelet associated.⁶⁴ As observed by Chernesky and others⁶⁴ and Larke and Wheelock,⁶⁵ mixing of human platelets with CHIKV leads to the sequestration of viral particles inside platelets aggregates in a way that stabilizes the infectivity of the virus. The sequestration is time dependent at 37°C. Therefore, the fact that the virus used in these studies is not produced *in vivo* does not appear to affect this property of the virus. It is not known whether the virus is physically located inside human platelets, or if the platelets aggregate and form a protective coating for the viral aggregates.^{64,65} The results of similar studies of the photochemical inactivation of CHIKV using riboflavin and UV light (Mirasol Pathogen Reduction [PR] System) in platelet components in platelet additive solution and in plasma components were recently published by Vanlandingham and others.⁶⁰ Using the same strain of CHIKV used in the platelet studies presented here, 2.2 and 2.1 log reduc-

tions of CHIKV infectivity were observed in platelets and plasma, respectively, treated with the Mirasol system. Interestingly, higher inactivation was observed in cell culture media indicating an inhibitory effect on the Mirasol PR system in the presence of plasma and platelets. This may indicate protein interference or it may be a result of the known sequestration of CHIKV in platelets. This is in stark contrast to the results obtained for this study, where high levels of inactivation were achieved in the presence of platelets and of plasma, and may be the result of mechanistic differences between the two systems.

Considering that human viremia does not reach levels higher than 5–7 log₁₀TCID₅₀/mL^{1,60,65–67} in ill individuals, it appears that this technology will result in complete inactivation of the presumably even lower levels of CHIKV in platelet and plasma components collected from asymptomatic donors. Even though it is impossible to guarantee that an infectious titer exceeding the capacity of the system will never occur, INTERCEPT inactivation of more than 5–6 log titers offers a significant risk reduction for transfusion-transmitted infections with these pathogens. This is especially pertinent in light of recent evidence that lower titer CHIKV viremia may be associated with different clinical outcomes than high titer viremia³⁶; additionally, routine use of the pathogen inactivation system may be a viable alternative to the deferral of donors that have traveled in CHIKV endemic areas provided they meet the other screening criteria.

In northern Italy, all blood donations were halted during the CHIKV outbreak and this resulted in an economic loss exceeding 3 million euros^{1,31} caused by the expense of importing blood to sustain a local supply. In this regard, photochemical treatment of blood products with amotosalen and UVA could significantly reduce the risk of CHIKV transmission, and thus, represents an attractive means to prevent the disruption of a local supply of blood products in the affected areas during CHIKV outbreaks. This is particularly true of platelets because of their limited shelf life of 5 days.⁶⁸ This theory was put into practice during the La Réunion outbreak when, in 2006, French authorities implemented mandatory photochemical treatment of platelet components with the INTERCEPT Blood System to reduce the risk of CHIKV transmission on La Réunion.³² Approximately 4,000 platelet units were administered over the course of 1 year, and no transfusion related CHIKV transmissions were documented. Although pathogen inactivation obviously adds cost to blood components, in the context of the current testing paradigm and assuming that there is no established nucleic acid test assay for a specific pathogen, it has been found that pathogen inactivation is more cost effective than NAT in terms of quality-adjusted life years, a measurement of clinical and cost effectiveness. Additionally, it has been recognized that pathogen inactivation can also be seen as an insurance policy against other chronic or acutely transmitted pathogens.⁶⁹ The INTERCEPT system is in fact already in use in 17 countries and under evaluation in additional areas in which CHIKV and other pathogens are endemic or epidemic.⁷⁰

In summary, our study shows that photochemical treatment of human apheresis platelet concentrates and plasma components with amotosalen and UVA results in efficient inactivation of high levels of CHIKV that would reduce or eliminate transfusion-transmitted infection. This suggests that photochemical treatment of platelet or plasma components would be an effective method for prevention of transfusion-transmitted CHIKV infection in the areas of CHIKV endemic/epidemic activity.

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