
STAYTECTM Enhanced Insect Repellent

White Paper

Abstract

Mosquito repellents have been around since World War II with minimal improvement in technology. The failure of products to meet the real users' needs, has led to a very low adoption in using topical insect repellents as a vector control intervention throughout the Global South. The World Health Organization (WHO) currently has a recommendation against topical repellents at the community level, due to lack of evidence around individual compliance and adherence to affect community level spread of diseases such as malaria.

Currently the approved interventions to combat malaria in the Global South are Long-Lasting Insecticidal-treated Nets (LLIN) and Indoor Residual Spraying (IRS). These are acceptable indoor tools. However, neither of them are effective outdoors, and evidence is mounting to indicate an increase in malaria carrying mosquitoes biting earlier in the evening and later into the morning, at times when individuals are not protected by an ITN in their bed or inside their house. This raises the need for a new type of mosquito repellent that solves both the compliance and adherence challenges faced by policy makers, like the WHO, when considering the endorsement of repellents as a public health intervention.

This new type of mosquito repellent is available today and the first example of this next generation of repellents called Enhanced Insect Repellents (EIRs) includes STAYTECTM with 20% IR3535[®], which is proven to reduce malaria carrying mosquito bites in both field and laboratory studies. To improve both effectiveness and safety, STAYTECTM is a patented technology designed to control the release of IR3535[®] and reduce absorption into the skin. By applying it to IR3535[®] it makes the safest EPA-approved repellent active even more safe as it stays on skin longer. Lastly, it's able to be formulated as a pleasantly scented lotion that dries quickly, leading to better adherence.

LivFul's Enhanced Insect Repellent (EIR), using the STAYTECTM technology with IR3535[®], was studied as a possible intervention against malaria and potentially against other vector borne diseases. Arm-in-cage and field studies efficacy tests were conducted with the repellent, showing an average protection time of 14 hours (Brazilian ANVISA and US EPA guidelines). In addition, an overnight semi field study conducted in a malaria endemic area in Ghana, showed a significant reduction of 98% in the landing rates during 9 hours, including mosquitoes with pyrethroid resistance. This study also showed a significant impact in the entomological inoculation rate in those individuals treated with LivFul's STAYTECTM EIR.

Additionally, consumer surveys have shown that 93% of participants "definitely want" to keep using LivFul's EIR product, and a 45 day trial in Ghana reported zero cases of malaria in a sample of 100 security guards that contracted malaria at a 73% rate in the previous 12 months. One of the trials resulted in a 100% elimination of malaria cases among participants, saving a total of 160 sick days. This intervention shows significant potential as part of daily skin care routine with no need for reapplication, no side effects and could significantly contribute to the elimination of malaria and other insect-borne diseases.

STAYTECTM is a patented technology designed to control the release of IR3535[®] on the skin.

1. Introduction

According to the World Health Organization, vector-borne diseases “account for more than 17% of all infectious diseases, causing more than 700,000 deaths annually,”ⁱ with malaria accounting for an estimated 80-90% of those deaths.ⁱⁱ Every 40 seconds, a child somewhere around the world dies from malaria.ⁱⁱⁱ Unfortunately, progress in reducing malaria mortality and morbidity has levelled off, particularly in countries that carry a high burden of the disease.^{iv}

The WHO’s Global Malaria Program Operational Strategy 2024–2030 identifies “new tools and innovation” as one of five key pillars to achieve the goals set in the Operational Strategy as traditional interventions such as Long-Lasting Insecticidal Nets (LLINs) and Indoor Residual Spraying (IRS) efficacy rates decline.^v Additionally, for other vector-borne diseases, LLINs are not an effective intervention because the mosquitoes that carry such diseases bite during the day, as LLINs are effective only when a person is below the net during sleeping.

Historically mosquito repellents have proven inconclusive as an effective prevention tool in community wide studies for vector control.^{vi} Discussions with vector control experts indicate this has primarily been due to problems with adoption and adherence during studies – people don’t like using the current mosquito repellent options on a daily basis. A new generation of topical mosquito repellent called Enhanced Insect Repellents (EIRs) has been developed, performing above standards in safety, effectiveness, and user experience. Studies demonstrated that adoption and adherence issues could be overcome, leading to EIRs becoming a viable tool to combat vector borne diseases.

1.1

Vector-borne diseases

~249 million

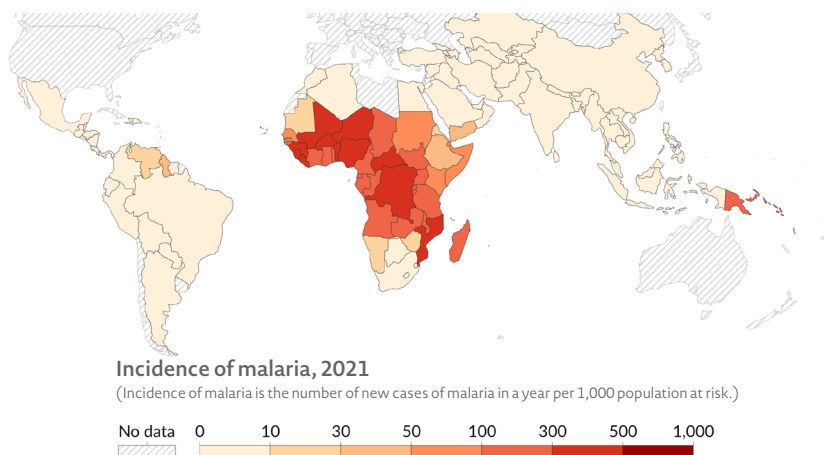
estimated malaria
infections occurred
in 2022

Mosquitoes are considered “disease-carrying” due to the female’s bloodsucking habit. They transmit diseases such as zika virus, malaria, dengue fever, and yellow fever when the female takes a blood meal.^{vii} One of the most urgent global health concerns in vector-borne diseases control is eliminating risk for economically disadvantaged populations in tropical areas where mosquito-spread diseases are concentrated.

1.1.1 Malaria

According to the 2022 World Malaria Report:^{viii}

- Nearly half the world’s population lives in areas at risk of malaria transmission in 87 countries and territories.
- There are 84 malaria endemic countries and territories. In 2022 there were an estimated 249 million cases and 608,000 deaths, of which 95% of cases and 96% of deaths were in the WHO African Region.



<https://ourworldindata.org/grapher/incidence-of-malaria>

More options are needed to keep those at risk less vulnerable. As an example, malaria is both endemic and perennial throughout Uganda which has one of the highest global burdens of malaria cases. Over 90% of the population is at risk, with malaria constituting Uganda’s leading cause of death, especially in children. In 2022, WHO reported that there were an estimated 12.7 million malaria cases and over 17,556 estimated deaths in the country.^{ix}

Even when treated immediately, malaria can debilitate a person for days, sometimes weeks—plaguing the host with fever, nausea, chills, fatigue, and muscle aches. Malaria not only causes physical suffering for the individual infected but restricts their ability to care for family and go to work, and can cause chronic absenteeism for students, and the constant feeling of being behind academically. According to the US National Institute of Health, another risk for children is that severe malaria can cause permanent brain damage, creating lifetime challenges.^x The economical burden of malaria is also considerable.

400 million

Dengue Fever
infections occurring
annually

~170,000

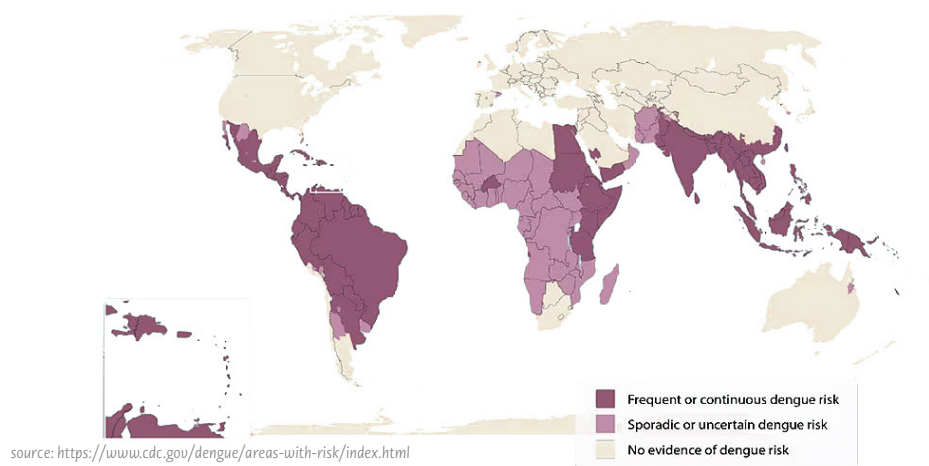
Yellow Fever
infections occurred
in 2023

Achieving the World Health Organization (WHO) target of reducing malaria by 90% by 2030 would not only avert 600,000 deaths annually, but could also increase Africa's GDP by \$16 billion per year.^{x(b)}

Additionally, people with malaria are more attractive to mosquitoes, which exacerbates the transmission, and keeps human bloodstreams as hosts for malaria, a cycle that is hard to break without the right combination of treatment and protection.^{xi}

1.1.2 Dengue Fever

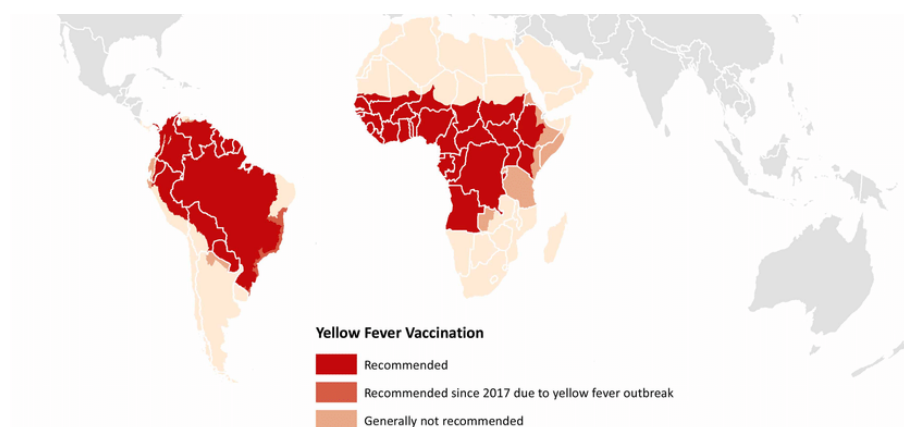
The WHO reports that approximately half of the world's population is at risk of a dengue fever infection, with as many as 400 million infections occurring annually.^{xii} 2024 set new global records for the most amount of dengue infections.^{xii(b)} Most cases are asymptomatic, but severe cases involve debilitating pain, fever, nausea and severe rashes, and death. There is no treatment for dengue so limiting incidence through vector control tools is the main way to limit infections.



The mosquitoes that spread dengue fever bite during the day, so personal protection is the primary method of disease prevention.

1.1.3 Yellow Fever

The WHO also reports that in 2023, 47 countries in the world reported cases of Yellow Fever, with estimates of between 84,000 and 170,000 severe cases leading to 29,000 to 60,000 deaths in Africa. This is despite the availability of a vaccine that grants lifelong protection from infection. Like dengue fever, yellow fever is caused by the bite of day-biting mosquitoes.^{xiii}



1.2 Tools to mitigate vector-borne diseases

Long-Lasting Insecticidal Nets (LLINs) are bed nets that are treated with an insecticide that kills the mosquito when it lands on the bed net. LLINs have a dual purpose of physically preventing the biting of the person under the net, as well as killing the mosquito when it lands.^{xiv} Indoor residual spraying (IRS) involves coating the walls and other surfaces of a house with an effective insecticide to kill mosquitos when they land on the walls.^{xv} Both interventions have demonstrated efficacy in reducing the transmission of vector-borne diseases in endemic settings. Public concern about diseases transmitted by mosquitoes in Africa has increased conspicuously. As an effect of climate change, malaria-carrying mosquitoes are tending to bite longer (pre-dusk, post-dawn) meaning there is a greater need for outdoor protection, especially amongst the most vulnerable (pregnant women and young children).^{xvi}

Topical insect repellents have had limited success as a vector control intervention. Though current repellents offer some “on-the-go” protection, to date, there has not been an affordable and accessible repellent on the market that meets three most-needed use characteristics: (i) good user experience, (ii) all day efficacy, and (iii) safety. Typically, repellents may have one or two of these characteristics, but not all three in one product. This has led to low user adoption in areas with high vector-borne disease prevalence. However, interest in repellents has risen due to the mosquito’s resistance to pesticides, leading to more outdoor biting.^{xvii}

1.2.1 Current Interventions

Long-lasting Insecticide-treated Nets (LLINs) and IRS (Indoor Residual Spraying) remain the main strategies for vector-borne disease control around the world and through their use, much progress has been made in reducing the malaria burden globally. However, with the recent evolution of pyrethroid resistance in *Anopheles* and the changing behavior of malaria vectors in Africa, the prospect of reduced efficacy of insecticide-treated bed-nets for preventing disease highlights the importance of strengthening the available arsenal of personal protection measures and novel interventions in supporting the disease elimination agenda in the sub-continent. A recent study indicated that an increase in early evening biting could increase transmission because people are unprotected by nets.^{xviii} Current topical insect repellents have been available in high income countries for decades, but their application to infectious disease problems in low-middle income countries has been frustrated by doubts about their adoption for daily use.^{xix,xx}

1.2.2 Topical Insect Repellents

Repellents could fit as a new intervention into the future of an integrated approach to malaria eradication in the Global South, yet average adoption rates of topical repellents often hover around 10% of the population. A majority of this 10% are among the wealthiest and most educated citizens, those who are less likely to suffer from malaria’s most serious effects. With this population, repellents are rarely used, often 3 to 10 times per year, which is not often enough to move toward disease eradication.

For the larger 90% of the population of Sub-Saharan Africa, repellents have not been successful thus far. What will make repellents work for this population is a careful balance between investment in repellent resources by governments and the private sector and grassroots-level programs by local health officials that will educate the public and encourage them to use repellents daily as part of a regular hygiene and wellness routine. This can be accomplished by making personal repellents easy to use and integrate into one's daily routine and providing extremely effective results.

The future of malaria prevention lies in empowering individuals to use products that they can incorporate into their daily routines that will consistently protect them from mosquito bites, giving them the freedom to enjoy outdoor (and indoor) activities without risking and falling ill to mosquito-borne diseases.

In addition, a new way to measure repellents' usefulness from a public health and global health perspective is needed. The current measure is solely based on efficacy, but in the context of public health, adherence, adoption, and affordability are also key. A new comprehensive calculation that would measure repellents' likelihood to be safe for daily use and likeability (smell, feel), with a potential metric such as viscosity, olfactometer, and standards for safety are needed. Like Sunscreen Protection Factor (SPF), there needs to be a harmonized approach in the repellent industry that combines these metrics into one score that helps the consumer make choices about repellents and pushes the industry to design better products for public good.

1.2.2.1 Enhanced Insect Repellents (EIR)

Most of the current efforts to improve repellents are focused on creating a new active ingredient, which is time intensive and costly, and does not eliminate human suffering and improve quality of life quickly enough. New ingredients require lengthy long-term environmental studies and regulatory processes in each market, which can take up to several years. This is then followed by lengthy finished product registration that ranges between 1-4 years depending on the market.

Enhanced Insect Repellents (EIR), however, take a different approach by utilizing existing natural and synthetic active ingredients (AIs) that are already well studied and proven to be effective, known in the industry, familiar to public health experts and policy makers. EIR uses controlled-release and other similar additive technologies to improve their efficacy, safety, and user experience to meet the needs of Global South consumers.

The next generation repellents, EIR, are here and poised to be a new industry standard. This transition presents an opportunity to create new standards on how to measure the performance of repellents based on more than just efficacy. A new standard that seeks to measure safety for daily use and user friendliness for a much more comprehensive performance measure. This sort of measurement would better align the industry's product development behavior with public health good. It may be like the advancements of SPF in the sunscreen industry. A singular score that could appear on the product label, making it easy for consumers to purchase the correct level of protection.

98%

reduction in mosquito landings on skin with the use of STAYTEC™ with 20% IR3535®

100%

elimination of malaria cases was achieved in one of the trials, saving a total of 160 sick days

Enhanced Insect Repellents with STAYTEC™

A well-executed approach of this type could unlock new market opportunities for the industry and go beyond the current penetration rate of less than 20%. A bigger and faster growing market attracts the best chemical and consumer health companies to enter the market leading to better products and marketing spend that will advance consumer awareness and education.

Successful laboratory and field trials have produced the following results:

- The use of STAYTEC™ with 20% IR3535® reduced mosquito landings on skin by 98%.
- The EIR lotion and wipes had an average complete protection time of 14 hours.
- 93% said they would “definitely want” to keep using the product after the trial, 96% said the repellent was extremely effective or effective, 98% said they liked the repellent, and 100% said they never, or rarely, had bites with the repellent, leading to a 99% satisfaction rate with this group. 94% would pay out of their own pocket for the product going forward and would use it every day.
- There was a 100% drop in malaria cases for participants and zero sick days for malaria cases during the trial, which eliminated 160 combined sick days for employees using the product.
- Over sixty-nine percent will use STAYTEC™ with 20% IR3535® every day once they purchase the product. The majority of users (73%) prefer to purchase the product from shops close by within their communities.
- At the beginning of the trial, 100% of participants tested positive for malaria. At the end of the trial 26 of 31 participants tested negative for malaria, effectively controlling the spread of malaria.

With the adoption of the next generation of repellents, people in the most malaria-prone areas will benefit from daily use of an easy-to-apply mosquito prevention product. However, public-private partnerships are needed to educate the public, making the product easily accessible and affordable.

LivFul has developed and tested the next generation of solutions that will prevent mosquito bites, the spread of malaria, and all the inconveniences that they cause. The development of this Enhanced Insect Repellent (EIR) is the solution that emerging countries need as part of the public health and economic growth plan.

The first example of this next generation of repellents called EIRs includes STAYTEC™ with 20% IR3535®, which is proven to reduce malaria carrying mosquito bites in both field and lab studies (cf. 2.2 and 2.3). By using existing active ingredients, those most at risk for contracting malaria can be protected much sooner than waiting for new active ingredients to be developed, as regulation is a long, tedious, and expensive process involving environmental and human studies, and ingredient registration around the world. This is followed by a similar process for the end-product consumers will use.

For the first EIR product LivFul chose to partner with Merck KGaA due to the favorable safety and cosmetic profile of their API, IR3535®. Natural active ingredients lack longevity^{xxi}; users must reapply multiple times per day for maximum effectiveness. In addition, in many places around the world, effective ingredients such as DEET, Picaridin, and oil of lemon eucalyptus often come with age restrictions.

1.2.2.1.1 Active Ingredient

The active ingredient, IR3535[®], is a technical grade synthetic biochemical that is produced by an integrated process. IR3535[®] has been shown to be safe for use by pregnant women and babies two months of age or older.^{xxii,xxiii} The molecule has an excellent environmental safety profile: it's nontoxic to aquatic organisms (fish, daphnia, algae), it's not persistent or bioaccumulating in the environment and it's biodegradable.^{xxiii} Studies have shown IR3535[®] repellents to be effective against Mosquitoes of the genus *Culex*, which carry West Nile virus, *Anopheles*, which carry malaria, and *Aedes*, which carry dengue fever, Zika virus, chikungunya, and yellow fever. Other studies have established that the repellency after application lasts between four and 10 hours, depending on the formulation, the applied dose and mosquito species tested.

1.2.2.1.2 STAYTEC[™] with 20% IR3535[®] Technology

The combination of IR3535[®] and STAYTEC[™], brings to life a next generation repellent that is safe, and provides effective protection from insects for everyone.

STAYTEC[™] with 20% IR3535[®] is LivFul's patented controlled-release technology of the active ingredient ethyl butylacetylaminopropionate used in the manufacturing process of enhanced insect repellents. Basically, the micro-encapsulation of STAYTEC[™] with 20% IR3535[®] is achieved emulsifying a water-immiscible core including charged polymers in water which form a capsular wall at the droplet interface of the oil/water emulsion.

This EIR is safe to use for anyone over two months of age and pregnant women, and the product poses no environmental harm. The chemical name of the active ingredient IR3535[®] is ethyl butylacetylaminopropionate, which has been used in repellent products in Europe for more than 30 years. It has also been registered with the EPA. There have never been reports about serious side effects from the use of IR3535[®]. The active ingredient is safer than other active ingredients such as DEET or Picaridin or Oil of Lemon Eucalyptus.^{xxiv,xxv}

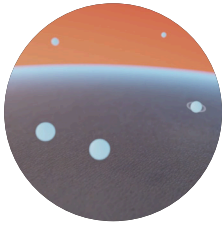
STAYTEC[™] is an innovative standalone technology and can be combined with almost any active ingredient. As an EIR, it fits easily into people's daily wellness routines in several ways: ease of application, comfortable on skin, and hours of protection following application. Cosmetic features of IR3535[®] make it ideal to customize and fit into people's daily lives. Odorless with a smooth feel, the product quickly dries onto the skin, and manufacturers can customize both scent and feel of the product.

1.2.2.1.3 STAYTEC[™] EIR Properties

LivFul has created the next generation in malaria prevention, Enhanced Insect Repellent (STAYTEC[™] with 20% IR3535[®]), that works powerfully without compromise. It uses IR3535[®], the safest repellent active recognized by WHO. The enhanced insect repellent is gentle, long-lasting, DEET-free, and hypoallergenic*, utilizing STAYTEC[™] technology for 14 hours of protection. The EIR is safe for all-day, everyday use for the outdoor workers, but also children (two months and older) and pregnant women.

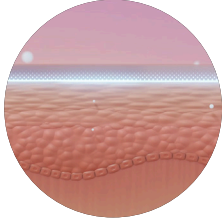
IR3535 is a registered trademark by Merck KGaA, Darmstadt, Germany

* The product contains low levels of cetyl alcohol and trace amounts of allergens



Slow Release

STAYTEC™ patented technology is designed to control skin absorption and evaporation of the active repelling agent. This means that the repellent does not evaporate rapidly, but in a controlled manner, enabling a long-lasting repelling action of up to 14 hours.



Reduced Skin Penetration

STAYTEC™ patented technology is designed to limit the active repelling ingredient penetration of the skin: enabling the full quantity of agent to be used as repellent and not “wasted,” increasing safety. The formulation is designed with the intent to reduce the rate of absorption into human skin.



Soft Touch

STAYTEC™ patented technology contributes to the formulation of a soft emulsion with a skin neutral pH. After a smooth and pleasant application, the lotion virtually disappears, leaving an invisible protection that is not sticky, greasy, or smelly.

Safety

In addition to the high safety of the active ingredient used in the Enhanced Insect Repellent (STAYTEC™ with 20% IR3535®) (see corresponding section), the Enhanced Insect Repellent has also been proven to be safe for topical use on human skin. This is based on the assessment of the acute systemic toxicity of the product as well as other skin compatibility tests such as dermal sensitization, phototoxicity, and photosensitization tests. All these tests have been conducted by independent laboratories and have proven an excellent toxicological and safety profile for the insect repellent.

A summary of the more recent toxicological tests conducted for the Enhanced Insect Repellent are shown below:

1. Dermatological evaluation of topical compatibility primary and accumulated dermal irritability (HRIPT):

Performed by Laboratorios Ecolyzer LTDA., Sebastião Mazzoni Street, 263 in São Paulo, Brazil in December 2023, according to the ANVISA Safety Assessment Guide, 2012, with 55 participants. Conclusions: the data obtained demonstrated that the product did not induce any process of primary dermal irritability, accumulated dermal irritability or sensitization. Being the product safe for topical use in accordance with the ANVISA Safety Assessment Guide, 2012 and therefore considered, “Dermatologically Tested, Clinically Tested, Primary Dermal Non-Irritant, Accumulated Dermal Non-Irritant, and Non-Dermal sensitizer”.

2. Dermatological evaluation of topical photoirritant and photosensitizing potential in humans:

Performed by Laboratorios Ecolyzer Laboratorios Ecolyzer LTDA., Sebastiao Mazzoni Street, 263 in Sao Paulo, Brazil in December 2022, according to the ANVISA Safety Assessment Guide, 2012, with 26 participants per test. Conclusion: the product did not induce any potential for photoirritation. The product was considered safe for topical use in accordance with the ANVISA Safety Assessment Guide, 2012 and therefore considered 'hypoallergenic'.

3. Dermatological test (semi-open extended test):

Performed by ITA TEST Laboratorium, Obozowa 82a Ita-Test Sp. Z O.O. Research Laboratory, 01-434 Warsaw, March 2023, according to test procedure 07/DA ITA – TEST, ed. 1 of on 20.03.2005, by a dermatologist in the group of 40 volunteers by a contact test – a semi-open extended test. Conclusion: On the basis of results of the conducted semi-open contact tests, it was concluded that the product tested met the requirements of compatibility with skin (skin compatibility tests).

4. Dermatological test (semi open extended test RIPT):

Performed by ITA TEST Laboratorium, Obozowa 82a Ita-Test Sp. Z O.O. Research Laboratory, 01-434 Warsaw, March 2023, according to test procedure 07/DA ITA – TEST by a dermatologist in the group of 50 volunteers by a RIPT contact test. Conclusion: On the basis of results of the conducted semi-open contact tests, it was concluded that the product tested met the requirements of the compliance RIPT test (skin compatibility test) and met the requirements of the cosmetic qualities to the declared properties so-called hypoallergenic.

5. Acute Oral Toxicity in Rats:

Performed by Stillmeadow Inc., 12852 Park one drive, Sugar Land, TX 77478, June 2022, according to OCSPP 870.1100 and OECD 425 guidelines. Conclusion: Acute oral LD50 > 5000 ppm in female albino rats.

6. Acute Dermal Toxicity in Rats:

Performed by Stillmeadow Inc., 12852 Park one drive, Sugar Land, TX, June 2022, according to OCSPP 870.1200 and OECD 402 guidelines. Conclusion: Acute dermal LD50 > 5050 ppm in male and female albino rats.

7. Acute Eye Irritation in Rabbits:

Performed by Stillmeadow Inc., 12852 Park one drive, Sugar Land, TX, July 2022, according to OCSPP 870.2400 and OECD 405 guidelines. Conclusion: The test substance is moderately eye irritating. Since all positive effects cleared by 48 hours, the test substance is assigned Toxicity Category III. No effects were observed in any eye on day 7.

8. Acute Skin Irritation in Rabbits:

Performed by Stillmeadow Inc., 12852 Park one drive, Sugar Land, TX, June 2022, according to OCSPP 870.2500 and OECD 404 guidelines. Conclusion: The test substance is qualified as non-irritating. Based only on scores after 72 hours of observation, the substance is assigned Toxicity Category IV.

9. Skin Sensitization in Guinea Pigs:

Performed by Stillmeadow Inc., 12852 Park one drive, Sugar Land, TX, July 2022, according to OCSPP 870.2600 and OECD 406 guidelines. Conclusion: The test substance is not a sensitizer in guinea pigs.

10. Acute Inhalation Toxicity in rats:

Performed by Stillmeadow Inc., 12852 Park one drive, Sugar Land, TX, June 2022, according to OCSPP 870.1300 and OECD 403 guidelines. Conclusion: The acute inhalation LC50 for the testing substance was determined to be greater than 4.95 mg/L in male and female albino rats.

2. Independent Public Health Studies

Efficacy study of the Enhanced Insect Repellent (STAYTEC™ with 20% IR3535®) Formulation against mosquitoes in natural setting, performed by the Parasitology Department at the Noguchi Memorial Institute for Medical Research at the University of Ghana.

The study was carried out in Osrogba and Obom, two villages about two kilometers apart and about 25 kilometers from Accra, Ghana. The inhabitants in the community are mostly farmers and the houses are made typically of mud and cement walls. The trial site provides breeding sites all year round for *An. gambiae* s.l. mosquitoes, which constitutes about 94% of the mosquito population, and is a malaria vector.

The trial was carried out in 2023. On each evening of the evaluation, the test product was evenly spread over the exposed lower legs using gloves to avoid cross contamination between the treated area and the control. The test solution was placed in unmarked containers labelled by code.

Comparisons of mosquito landing rates between the control and treatment legs were performed and technicians studied the mosquitoes' behavior with subjects' four prevention-treated and four untreated legs over 16 nights. Through this method, mosquitos had the choice to land on both treated and untreated skin. Seventy percent of the time, mosquito landings were on untreated skin. The use of STAYTEC™ with 20% IR3535® reduced mosquito landings by 98%.

STAYTEC™ with 20% IR3535® formulation showed a 98 % reduction in landing rates over a 9 hours period.

	Hours	% reduction in landing rates
The hourly mosquito landing rate of <i>An. gambiae</i> s.l. against a STAYTEC™ with 20% IR3535® formulation	21.00-22.00	100
	22.00-23.00	98
	23.00-24.00	97
	24.00-01.00	99
	01.00-02.00	96
	02.00-03.00	98
	03.00-04.00	99
	04.00-05.00	98
	05.00-06.00	100
	Total	98

It also showed a significant decrease in the biting rate including mosquitoes with pyrethroid resistance (control untreated: 16.3, treated: 0.59 (nb bites/person/night)).

And a significant impact in the entomological inoculation rate based on sporozoites measure (control untreated: 24, treated: all negative (nb of infective bites/man/year)).

This means the use of STAYTEC™ with 20% IR3535® formulation will prevent infectious bites to persons in the community annually, providing significant protection against mosquito bites.

These are promising results against some of the most deadly and aggressive mosquitoes in the world.

The following bio-efficacy tests have been conducted with the original Enhanced Insect Repellent:

Efficacy studies

	TITLE OF THE STUDY	GUIDELINES
LABORATORY BIO-EFFICACY TESTS	Efficacy tests in a repellent product for mosquitoes - <i>Aedes aegypti</i> (Diptera: Culicidae)	OPPTS 810.3700 (July 7th, 2010): Insect Repellents to be Applied on Human Skin
	Efficacy tests in a repellent product for mosquitoes - <i>Aedes albopictus</i> (Diptera: Culicidae)	
	Efficacy tests in a repellent product for mosquitoes - <i>Anopheles aquasalis</i> (Diptera: Culicidae)	
	Efficacy tests in a repellent product for mosquitoes - <i>Culex quinquefasciatus</i> (Diptera: Culicidae)	
FIELD TRIAL BIO-EFFICACY TEST	Field evaluation of two topically applied insect repellents products containing STAYTEC™ with 20% IR3535® against mosquitoes in Florida	

These tests were performed according to the OPPTS 810.3700 methodology (July 7th, 2010), one of a series of test guidelines established by the Office of Chemical Safety and Pollution Prevention (OCSPP) (formerly the Office of Prevention, Pesticides and Toxic Substances (OPPTS) prior to April 22, 2010), United States Environmental Protection Agency (EPA) for use in testing pesticides and chemical substances to develop data for submission to the Agency under the Toxic Substances Control Act (TSCA) (15 U.S.C. 2601, et seq.), the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) (7 U.S.C. 136, et seq.), and section 408 of the Federal Food, Drug and Cosmetic Act (FFDCA) (21 U.S.C. 346a).

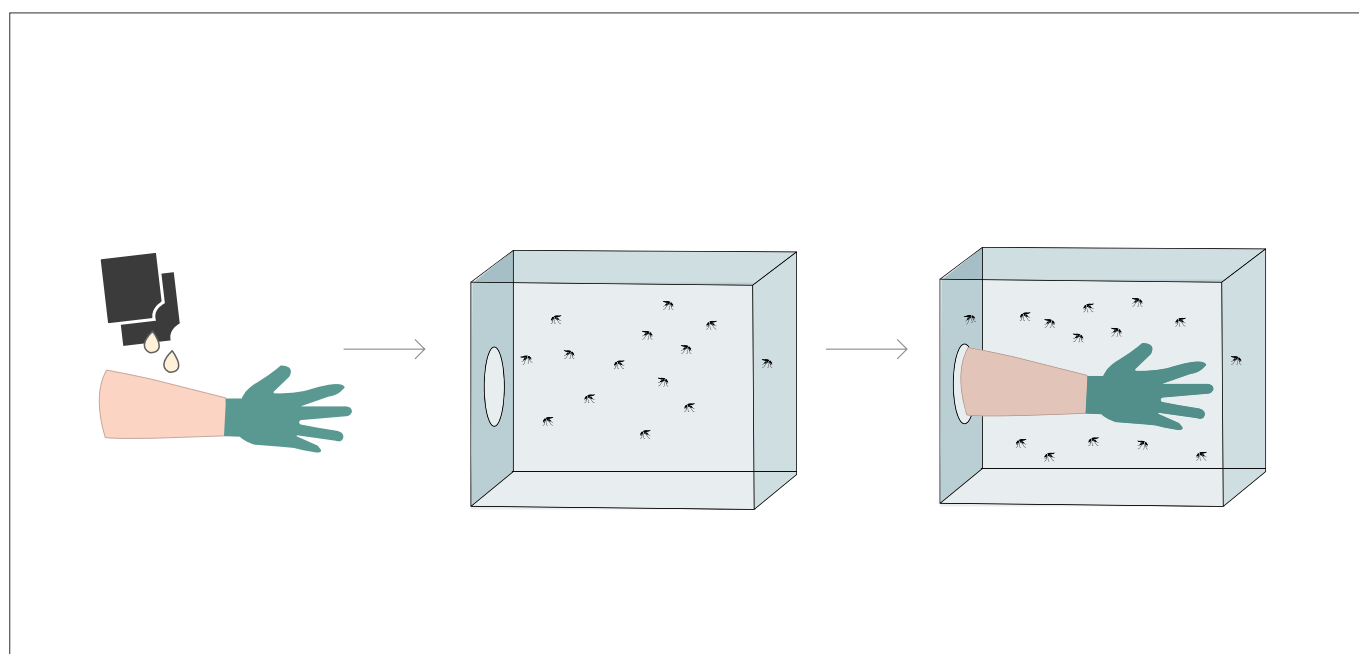
These are harmonized test guidelines which serve as a compendium of accepted scientific methods for research intended to provide data to inform regulatory decisions under TSCA, FIFRA, and/or FFDCA and provide guidance for conducting appropriate tests, and is used by EPA, the public, and the companies that are required to submit data under FIFRA. The methods described in these guidelines are strongly recommended for generating bio-efficacy regulatory data for use in testing pesticides and chemical substances.

2.1 Arm in Cage studies

Four tests were conducted with the original EIR against the mosquito species *Aedes aegypti*, *Aedes albopictus*, *Anopheles aquasalis* and *Culex quinquefasciatus* at Laboratorios Ecolyzer LTDA. (Sebastiano Mazzomi Street, 263 in Sao Paulo – SP – Brazil). The procedure followed and the results for each test are shown below:

Procedure:

Mosquitoes:	Host seeking females. 55 mosquitoes per cage (1 mosquito / 1160 cc).
Cages:	Acrylic, 40 x 40 x 40 cm (64000 cc).
Number of participants:	12 (2 untreated (mosquito attractiveness control), 10 treated with the EIR).
Dose applied:	2 sachets applied in the forearm.
Methodology:	Two groups of volunteers were used to test effectiveness. The untreated group was used to verify the mosquito activity (1 minute exposure or until 10 landings or bites every hour). The treated group exposed their arm for 5 minutes every hour until notification of the first bites. The longest time evaluated was 16 hours.



A brief process of efficacy testing of mosquito repellents for human skin in the laboratory

Aedes aegypti

Date: 27 MAR 2017

Results: In the EIR treated group, none of the participants suffered bites until 15 hours of testing. At this analysis point 4 of the 10 participants registered them. No times longer than 15 hours were analyzed.

Conclusions: In accordance with the results obtained in the test conditions, the EIR was considered satisfactory repellent action against *Aedes aegypti* mosquito species for a period of 14 hours after its application.

Aedes albopictus

Date: 28 MAR 2017

Results: In the EIR treated group, none of the participants suffered bites until 14 hours of testing. At this analysis point 3 of the 10 participants registered them. No times longer than 14 hours were analyzed

Conclusions: In accordance with the results obtained in the test conditions, the EIR was considered satisfactory of repellent action against *Aedes albopictus* mosquito species for a period of 13 hours after its application.

Culex quinquefasciatus

Date: 29 MAR 2017

Results: In the EIR treated group, none of the participants suffered bites until 15 hours of testing. At this analysis point 3 of the 10 participants registered them. No times longer than 15 hours were analyzed.

Conclusions: In accordance with the results obtained in the test conditions, the EIR was considered satisfactory for repellent action against *Culex quinquefasciatus* mosquito species for a period of 14 hours after its application.

Anopheles aquasalis

Date: 30 MAR 2017

Results: In the EIR treated group, none of the participants suffered stings until 14 hours of testing. At this analysis point 4 of the 10 participants registered them. No times longer than 14 hours were analyzed.

Conclusions: In accordance with the results obtained in the test conditions, the EIR was considered satisfactory of repellent action against *Anopheles aquasalis* mosquito species for a period of 13 hours after its application.

2.2 Field trial studies

A field trial bio-efficacy test for the original EIR was conducted at the University of Florida (UF) Mosquito Repellent Testing Lab in the UF Entomology and Nematology Department located at 970 Natural Area Drive, Gainesville, Florida 32611 USA, in collaboration with the Arthropod Control Product Test Centre (ARCTEC) at the London School of Hygiene and Tropical Medicine located at Keppel Street, London, WC1E 7HT, UK.

The author of this study was Dr Emma N.I Weeks. The study conduct, raw data and report were inspected by the Quality Assurance Unit (QAF) at UF Mosquito Repellent Testing Lab, UF Entomology and Nematology Department to determine the status of compliance with the study protocol and applicable laboratory standard operating procedures (SOPs). This study commenced on 18 May 2018, with the field study starting 15 August 2018 and completing 26 October 2018. The full study was concluded on 6 February 2019. The details of the study are shown below:

Objective:

Determine the efficacy and duration of two topically applied insect repellent products, a lotion and a wipe containing STAYTEC™ with 20% IR3535® (also commercially known as Akiva™ in Nigeria) at preventing landing by mosquitoes.

Procedure:

Participant selection:	38 participants, 20 males and 18 females, completed a test day. 7 males and 7 females, not including an additional participant of either gender, were present for each test day. All candidates chosen were between 18-55 years, either a non-smoker or refrained for 24 hours prior and during each test and underwent a mosquito attraction test (arm in cage against <i>Aedes aegypti</i>). 48-72 hours prior to each test day, the participants were advised not to apply any strong scented cosmetics 24 hours before testing. They were also advised not to drink, smoke or undergo vigorous exercise 24 hour prior to testing.
Dose applied:	1 g undiluted sample / 600 cm ² skin (lower leg).
Test mosquitoes:	For the controlled attractiveness (arm in cage) testing and aspirator training completed within a controlled environment, <i>Aedes aegypti</i> mosquitos were used. For the field test mosquitoes, two sites which were prevalent with mosquito activity but low risk of Zika virus were selected. At the test sites, mosquito pressure remained high enough to ensure that at least one control participant obtained 5 landings in 5 minutes. Once a mosquito had landed, they were collected without the risk of biting, identified and tested for pathogens. All the <i>Aedes</i> and <i>Culex</i> species collected were tested for Zika, West Nile virus, St Louis encephalitis and eastern equine encephalitis. All mosquito pools were tested and found negative for these diseases.
Test day procedures:	20 participants were invited to the test each day. For each day, 7 males and 7 females and the next person who arrived were checked in and selected as the test subjects for that day. The remaining 15 participants were randomly assigned to either the treatment group or untreated control group. If a participant underwent multiple test days, they were randomly assigned a group and test site for each instance. The skin area was calculated, and the individual's dose was applied to the test area, within the two-hour period of the first mosquito exposure. Prior to exposure of the participants, the untreated control group was exposed for 5 minutes or until 5 landing occurred, whichever happened sooner. This was to establish biting pressure. If the landing pressure was high enough, 5 landings in 5 minutes, then the site was accepted. Every 30 minutes, biting pressure was assessed over a 5-minute period. Only mosquitoes landing on the test site were recorded and collected. The test was concluded when 50% of the participants reported the first confirmed landing. The first confirmed landing is the first landing to occur

followed by a second landing within 5 minutes or a landing within an exposure slot with a second confirmatory landing in the next exposure period to confirm that the landing was the repellent failing and not a coincidence. The time in which the first confirmed landing occurred is the endpoint of the complete protection time for repellent action. Within 72 hours of the test concluding, all subjects were contacted to determine if any of the participants had experienced adverse effects.

Results

No adverse events, including serious adverse reactions, occurred throughout this study. All subjects reported to be in good health at each health check period. The results of this study are shown below calculated as a median complete protection time:

Test	Site	TS	Subjects		Median CPT (minutes)	Lower 95%CI (minutes)	Median CPT	Lower 95%CI
			Failed	Censored				
1	1	Akiva™ lotion	7	6	848	788	14h 8min	13h 8min
4	1	Akiva™ wipe	6	7	NC(>960)	724	NC(>16h)	12h 4min
5	2	Akiva™ wipe	7	6	846	738	14h 6min	12h 18min
6	2	Akiva™ lotion	7	6	910	818	15h 10min	13h 38min

NC= not calculable as only 6 out of 13 reached CPT= Complete Protection Time

The overall complete protection time (CPT) was calculated to be greater than 14 hours for both the lotion and the wipes, with one group not reaching the 50% confirmatory landings up to the end of the test at 16 hours. To calculate the complete protection time, the lowest median results were used. For the Akiva™ lotion, the complete protection time was 14 hours and 8 minutes and for the Akiva™ wipe, the complete protection time was 14 hours and 6 minutes. The complete protection time for both products was 14 hours.

During sampling events from 2 June 2018 until 29 August 2018, 1,413 mosquitoes were collected and identified from Site 1 JH. During sampling events from 22 May 2018 until 12 September 2018, 3,664 mosquitoes were collected and identified from Site 2 NATL.

Scientific Name	Site 1 JH	Site 2 NATL
<i>Aedes albopictus</i>	876	22
<i>Ochlerotatus infirmatus</i>	199	900
<i>Wyeomyia mitchellii</i>	108	0
<i>Psorophora ferox</i>	101	750
<i>Culex nigripalpus</i>	58	1171
<i>Ochlerotatus atlanticus/tormentor</i>	17	77
<i>Ochlerotatus triseriatus</i>	14	46
<i>Culex erraticus</i>	7	79

Continued

Scientific Name	Site 1 JH	Site 2 NATL
<i>Psorophora ciliata</i>	6	0
<i>Culex quinquefasciatus</i>	6	64
<i>Ochlerotatus fulvus pallens</i>	5	17
<i>Coquillettidia perturbans</i>	3	14
<i>Aedes vexans</i>	3	96
<i>Culex peccator</i>	2	0
<i>Culex restuans</i>	2	12
<i>Culex tarsalis/coronator</i>	2	282
<i>Mansonia dyari</i>	1	46
<i>Anopheles quadrimaculatus</i>	1	2
<i>Culex salinarius</i>	1	35
<i>Anopheles crucians</i>	0	14
<i>Psorophora howardii</i>	0	3
<i>Anopheles punctipennis</i>	0	1
<i>Orthopodomyia signifera</i>	0	3
<i>Anopheles walkeri</i>	0	1
<i>Ochlerotatus species</i>	1	0
<i>Culex species</i>	0	15
<i>Aedes species</i>	0	13
<i>Psorophora species</i>	0	1

Conclusions:

This study concluded that the EIR lotion and wipes had an average complete protection time of 14 hours regardless of the person using the repellent, study site and mosquito species present. The product was proven to be effective with a positive user experience.

2.3 Ghana studies



2.3.1 Context of Malaria in Ghana

In 2022, Ghana was one of the hardest-hit African countries for malaria infections. More than 5 million were infected that year alone, and nearly 12,000 died as a result.

2.3.2 Ghana Outdoor Workers

A nonprofit organization called CouldYou conducted a clinical trial from October 2022 to September 2023 with the help of a group of Ghanaian overnight security guards who frequently missed work due to their high numbers of malaria cases. Prior to the testing, 97% of the group reported that they always or often experienced insect bites, while the remaining 3% of this group occasionally or sometimes experienced mosquito bites. 95% believed mosquito bites affected their productivity at work. Nearly three-quarters of

the group had suffered malaria in the previous 12 months. Not only did this affect their health, but it also affected their company's ability to operate with a full staff.

2.3.2.1 Pre-study disease pattern

For instance, 73% of the guards contracted malaria, and an average of 3.7 days were lost each month per security guard to malaria in the previous 12 months. Twenty-five percent reported malaria cases strong enough that they to cause them to miss work, losing a total of 93 productive days for their employer. The remaining 75% of malaria cases were not severe enough to keep the employee home from work, but decreased their effectiveness during their shifts while they had malaria. LivFul administered a 45-day trial with 100 security guard participants. During this time, no security guards experienced a mosquito bite, and they reported zero cases of malaria. In addition, absenteeism due to malaria was reduced to zero days.

2.3.2.2 Post study results

Following the trial, 93% said they would definitely want to keep using the product after the trial, 96% said the repellent was extremely effective or effective, 98% said they liked the repellent, and 100% said they never, or rarely, had bites with the repellent. LivFul's enhanced repellent had a 99% satisfaction rate with this group. Ninety-four percent of them would pay out of their own pocket for the product going forward and would use it every day. In addition to the product's effectiveness, participants believed the product was affordable and easy to use.

2.3.2.3 Testimonials and comments from the guards

Said one participant, "Anytime I apply the wipes, it sees me throughout my night shift with no mosquito and other insect bites. I personally think it works more than the 16 hours you people talked of. It works very effectively because throughout my night shift yesterday, I didn't even bother to find out where my jacket was. This [working without jackets] never happened before you brought the wipes. A night shift without jackets meant doom."

2.4 Uganda studies



2.4.1 Context of Malaria in Uganda

Over 90% of Uganda's population is at risk of contracting malaria. In 2022, there were 12.7 million reported cases and over 17,000 deaths.

2.4.2 Ugandan consumer Adoption study

2.4.2.1 Asili farms

Asili Farms amasses more than 22,000 acres of farmland and employs over 200 people to grow maize, soybeans, oilseeds, and other grains. A group of Ugandan farmers, all employees of Asili Farms, experienced high numbers of malaria cases; in four years over

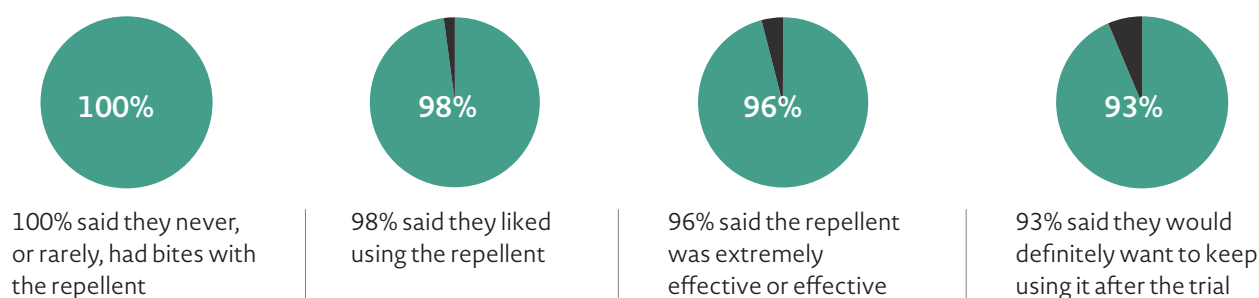
700 cases were reported, leading to over 2,800 total sick days and lost productivity for the farmers and the company. Each week, 10% of employees are out of work due to malaria, and the farmers contract 15 cases per month. Asili Farms spends \$621 per year on malaria treatment for their staff. Asili spent a total of 9.5MUgx on malaria medication and, by conservative estimate, lost 2,812 total days among sick workers in the last four years. Malaria not only causes physical suffering for the individual infected but restricts their ability to care for family and go to work.

2.4.2.2 Asili Farms 70-person study (pre-and-post study results)

Asili Farms signed on for a trial of LivFul's STAYTEC™ with 20% IR3535® Enhanced Insect Repellent for 73 of its employees over 60 days to determine if the repellent would prevent mosquito bites and the spread of malaria, thereby lessening the impact on both the employees and their families, and the company, its productivity, and bottom line. Employees participating in the trial were briefed and given 60 total sachets of lotion. Each sachet contains three milliliters of lotion to be applied once daily prior to arriving onsite in the morning. Asili Farms saw the benefit of moving to a preventative approach rather than reactive. Of the 73 participants, 11 were female and 64 were male; two of the participants dropped out of the trial before finishing.

The results of the study were very positive for the 73 participants: there was a 100% drop in malaria cases for participants and zero sick days for malaria cases during the trial. At this rate, Asili Farms will eliminate 160 sick days for employees using the product. Participants' adherence to and adoption of was extremely beneficial to employees and their employers.

Participant feedback was positive:



In a pre-trial questionnaire, the majority of participants responded that:

- Mosquito bites extremely affect or affected a lot their productivity and attention at work.
- Mosquito bites extremely affect or affect a lot their ability to sleep.
- Participants were always or often bitten by mosquitoes.
- Participants were extremely or somewhat satisfied or felt neutral about the scent and the feel of the product.
- Participants were extremely or somewhat satisfied or felt neutral about the product being skin-friendly and non-irritating.
- Every participant remarked that they are rarely or never bitten by mosquitos when using the repellent.
- All but three participants rated the product extremely effective or effective.
- Every participant reported that the repellent is easy or somewhat easy to apply to skin.

- All but one participant enjoyed using the repellent (one was neutral). Seventy of 75 planned to continue using it after the trial.

2.4.2.3 Asili Farms 200-person study (pre-and-post study results)

Asili Farms also partnered with LivFul for Phase Two of the study, reaching an even larger number of Asili Farms employees over a longer period. The study had very positive results and data is currently being analyzed.

2.4.2.4 CouldYou study seminar (pre-and post-study results)

CouldYou conducted a study in Uganda, despite a reduction in national under-five malaria prevalence from 30.4% in 2016 to 16.9% in 2018–2019, modelled projections, show that the country experienced approximately 12.3 million malaria cases and 13,203 malaria deaths in 2018, with little evidence of change since 2016. Malaria continues to contribute to 20–30% of all pediatric admissions to hospitals across the country, overwhelming emergency clinical services.

“Since I started using the repellent, I even see the mosquitoes around, but I never got any bite. The product is very good”

- Kaketo Moses (Uganda)

“Even though it effectively reduces mosquito bites, it doesn’t have any effect on the skin. It’s very comfortable”

- Sejjemba Ronald

Satisfaction of the product was tested as an important factor to ascertain the product’s acceptability. Following the proven effectiveness of the product, 98% are satisfied and all participants agree that STAYTEC™ with 20% IR3535® is a useful product. Some respondents elaborated that due to the effectiveness of STAYTEC™ with 20% IR3535®, they felt safe from the high risk of contracting malaria.

Experienced users are willing to purchase and use STAYTEC™ with 20% IR3535® frequently. 57% said they will purchase STAYTEC™ with 20% IR3535® every day if they find the product on the Ugandan market, and 69.4% will use STAYTEC™ with 20% IR3535® every day once they purchase the product. The majority of experienced users (73%) prefer to purchase STAYTEC™ with 20% IR3535® from close by shops within their communities.

The average price participants are willing to purchase a sachet of STAYTEC™ with 20% IR3535® repellent is 584 shillings (\$0.16).

2.5 Democratic Republic of Congo studies

2.5.1 Kuvuna Insect Repellent Trial - Congolese Children (The most vulnerable)



Through a partnership with the Kuvuna Foundation in the Democratic Republic of Congo, LivFul connected with Our Lady of Perpetual Help, an orphanage. In 2021, 31 people from the orphanage, 28 of them children and three of their caregivers, volunteered for a trial of STAYTEC™ with 20% IR3535®, to study prevention of mosquito bites and the

spread of malaria. All of the participants are always bitten by mosquitos; 29% contracted a case of malaria serious enough to be hospitalized. For those contracting malaria of any level of severity, 84% were ill from four to seven days, limiting their regular daily activities, including school attendance. Whether missing school or work, two-thirds of participants said they missed three to five days when sick. Students reported that mosquito bites affected their performance in school and the quality of sleep at night, which can also affect school performance.

Once the trial was underway, 97% of participants applied the repellent twice daily, and 100% of them did not receive any mosquito bites while using the repellent, showing the product's effectiveness. At the beginning of the trial, 100% of participants had the malaria parasite in their bloodstreams. At the end of the trial 26 of 31 participants had no malaria parasite in their bloodstreams, effectively eliminating the parasite and not being able to infect others.

After the trial's conclusion, participants using the repellent every day twice had not been bitten by mosquitos during the trial, remaining healthy, sleeping well, and appearing at school or work each day. One-third remained unbothered by mosquitos at night, while two-thirds reported being slightly affected by mosquitos at night. All 100% of participants loved the repellent, thought it worked well for them, and wanted to continue using it after the trial ended. Almost all participants (97%) thought the repellent was effective at preventing malaria.

2.5.2 Post-trial comments by participants included:

"Now I can play with my friends outside late in the evening with no mosquito bites."

"I can now focus on my studies with no worries of mosquito bites."

"I never seen a product like this before. I use it as a lotion and no more mosquitos around me or bite me. Every evening after my soccer practice, I take a shower and then apply this repellent. I go to sleep like a baby because there are no more mosquito bites."

"I have not missed work since I started to use this product. This product works and would recommend it to everybody. We have seen no more cases of malaria in our orphanage since we have started to apply this product. We have saved money from malaria treatment and now use the funds for more educational and nutritional programs."

2.5.3 The head caregiver reported that:

On average, the children's home will spend \$400 per month on children that have fallen ill from malaria. Four to five children typically fall ill from malaria in each month, with typical costs of treatment ranging from \$80-100 per child.

During 2020, they spent approximately \$1,200 during the first quarter on malaria treatment for the children.

In 2021, the orphanage spent nothing during the first quarter on malaria treatment for the children.

Overall, the participants at the orphanage respond positively to the repellent product.

2.5.4 School

From the pre-trial data, it can be deduced that potentially 19 days of school (or work) per year could potentially be lost due to a mosquito borne illness. Following the trial, no school had been missed and more importantly, 90% of participants in their view, were no longer impacted by the mosquito.

2.5.5 Savings

A statement from the Head Nurse confirms that potentially \$800 has been saved for the months February and March 2021. This would be savings from the money spent on malaria treatment which is estimated around \$80-100 per child. These were the months of which the children were subject to repeated repellent use.

The use of LivFul's Complete insect repellent seems to have prevented further illness of malaria during the test trial period, which would typically see four to five children falling ill in each month. There is potential indication from the data sources to suggest the repellent is preventing people there from contracting malaria.

"It is wonderful. The smell is mild, and my kids love it. It also works really well. My daughter, who generally attracts mosquitoes like a magnet, was bite free playing in the woods all afternoon...."

Amy K

Discussion

The next generation of EIR is here, and an industry standard is needed to help consumers decide on the right protection for them and their families. Through a system that labels repellent products with a repellent protection factor, or RPF, consumers can best protect themselves from mosquitos and stop the spread of malaria.

The active ingredient in our repellent is IR3535®. It has a strong safety profile that has been proven for more than 30 years.

The World Health Organization (WHO) stated, IR3535® is recommended as a safe and effective insect repellent for human use." This safety record makes it ideal for use by the whole family. IR3535® is effective against mosquitoes, ticks, fleas, lice, and sandflies.

STAYTEC™ with IR3535® is a unique and advanced DEET-free lotion. LivFul's STAYTEC™ technology enables this product to **meet three high standards**: it is **safe** to use, **effective** at preventing mosquito bites, and is **comfortable** to wear. It is this combination that makes STAYTEC™ with 20% IR3535® superior to current repellent products. It is hypoallergenic and suitable for children over two months old and pregnant women. It creates an invisible barrier of protection which is easy-to-apply yet powerful. Combining the patented controlled release technology to create a repellent that is designed to work longer. It is designed to help slow both evaporation and skin absorption of the active ingredient. The result is a long-lasting repellent with protection for 14 hours.

LivFul generates bottom-up insights built on local context, behavioral patterns of consumers and systemic challenges to understand what challenges to focus on, approximate ideal solutions, align resources to address them, and layout a long-term technology roadmap.

Conclusions:

The impact STAYTEC™ with 20% IR3535® has made to keep vulnerable populations safe from malaria has just begun, there is much more work to do. The products developed are safe and more effective than any other product currently on the market.

The need is to get this product in the hands of those who need it most and encourage them to make using STAYTEC™ with 20% IR3535® part of their daily routine.

For those who have already done this, the outcomes are tremendous: better health, better school and work attendance, increased productivity, a better lifestyle, and the freedom to enjoy more activities outdoors safely.

There is an effort to partner with governments and NGOs in areas where malaria is a risk, to bring this life-changing, safe and effective repellent to its population.

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