

## Target Malaria's insectaries

The laboratories where mosquitoes are kept, reared and studied in cages are called insectaries. Studying mosquitoes in insectaries helps researchers learn about their behaviour. For Target Malaria we are particularly interested in how genetically modified mosquitoes behave compared to wild type mosquitoes.

It is important to note that none of the Target Malaria's insectaries work with the malaria parasite or malaria-infected female mosquitoes.

### Work in the laboratories and insectaries

Target Malaria currently has laboratories and insectaries in the United Kingdom, Italy, Burkina Faso, Mali, Ghana and Uganda. The work taking place in each can differ, including the types of mosquitoes being handled.

#### Imperial College London, United Kingdom

Target Malaria started at Imperial College London as a university-based research programme. The work is focused on creating the genetic modification. It is created in the laboratory and then injected into mosquitoes in the insectary. The laboratory is separate from the insectary. The work in London also includes assessing whether, once inserted, the genetic modification can be maintained for several generations in a small cage (17cm x 17cm or 30cm x 30cm) population, without negative impacts on the mosquitoes.



#### Polo d'Innovazione di Genomica Genetica e Biologia (POLO GGB), Terni, Italy

Target Malaria's insectary in Italy is based in Polo d'Innovazione di Genomica Genetica e Biologia (PoloGGB) in Terni. Polo GGB has been working with universities, companies and diagnostic laboratories since 2011, but this facility was purpose-built for Target Malaria in 2016.

The insectary houses four "climatic chambers". These chambers are equipped with the latest technology to mimic the natural ecological conditions of the mosquitoes' species being studied (precise regulation and variation of light, temperature and humidity). Two of the chambers are used for rearing the mosquitoes in small, standard cages (0.005 m<sup>3</sup>). The other two chambers are fitted with 9 large cages (up to 9.2 m<sup>3</sup>) that are used for experiments. Such cages are built with sliding panels, so they could be resized to fit different study designs. They are big enough to accommodate thousands of mosquitoes, allowing for the study of large or small mosquito populations in conditions as close as possible to being "outside", while still being in a contained environment. Large cages also allow the study of important biological parameters, such as swarming and complex mating behaviour, which are not possible in small cages.

The main work of the laboratory in PoloGGB is to import wild strains of mosquitoes from Africa and transfer the genetic modification from the lab strain into the wild one. We then analyse the behaviour and characteristics of Target Malaria's modified mosquitoes, to determine whether they behave like wild mosquitoes and whether they could survive in the wild. Data collected on the modified mosquitoes in these large cages is compared with the information received from the teams doing entomology studies in Africa. These studies are very important to better understand the technology and to inform the regulatory process for import and release in Africa.

## Insectaries in Africa

- **Institut de Recherche en Sciences de la Santé (IRSS), Bobo-Dioulasso, Burkina Faso**
- **Malaria Research and Training Center Université des Sciences Techniques et Technologiques de Bamako (MRTC-USTTB), Mali**
- **Uganda Virus Research Institute (UVRI), Entebbe, Uganda**

Target Malaria currently has three teams working towards potential studies of modified mosquitoes in their facilities. In Burkina Faso, the team is at the Institut de Recherche en Sciences de la Santé (IRSS), in Mali the team is at the Malaria Research and Training Center (MRTC-USTTB), and in Uganda the team is at the Uganda Virus Research Institute (UVRI).

In all cases, the teams have upgraded or added new facilities specifically to carry out their research, as well as building their staff's knowledge and capacity to work with genetically modified mosquitoes. The research is subject to approvals by the national authorities, who regularly review the work being undertaken and give permission for specific activities.

Each team has an insectary and a laboratory allowing the teams to conduct analyses on the wild mosquitoes collected by the entomology teams in the field. When mosquitoes are collected in villages, they are taken to the laboratory where they are examined.

A record is kept of how they were caught, how many of them there were, and if they held eggs. The data contributes to understanding local mosquito population dynamics and to informing modelling and genetics studies. It also contributes to the identification of possible field sites for evaluating a gene drive mosquito in the future.

Once a team starts to work with a genetically modified mosquito strain (with the permission of national authorities), the insectary is where the team carries out their regulated studies. They will evaluate the presence and stability of the genetic modification over several generations and evaluate the mosquitoes' rearing behaviour (such as development time, number of eggs produced by females and proportion of eggs that successfully hatch and subsequently develop to adults). These characteristics are compared to wild type mosquitoes and are essential to inform the design of field evaluation studies if the research progresses and these are approved.

- **University of Ghana, Accra, Ghana**

The team at the University of Ghana is carrying out different work to the teams in Burkina Faso, Mali and Uganda. The Ghana team is working to understand the ecology of Anopheles mosquitoes and to improve capacity for the rearing and transport of mosquitoes.

For the ecology study, the team carries out field surveys, they analyse which mosquito predators are present, as well as study the content of those predators' guts to understand how the mosquitoes fit into the food chain.

The teams are also trying to understand what, if any, role mosquitoes play as pollinators in the environment.

To study rearing and transport, the team is building a specific facility, that will allow them to develop the best methods for rearing, handling and transport of male mosquitoes, such that they do not negatively affect their survival and ability to mate. The size of the cages used during these studies will vary: small cages, through to larger semi-field cages and field cages. None of this work involves genetically modified mosquitoes but rather locally caught and colonised mosquitoes.

## Safety measures in the insectaries

Safety is paramount to Target Malaria. Our teams work with experts and regulatory authorities to ensure we meet all the requirements for carrying out our research. All our insectaries meet the international guidelines and national regulations for the containment of insects, called "Arthropod Containment Level 2 (ACL-2)".

Level 2 containment means that there are specific measures in place to ensure mosquitoes cannot escape, and that external mosquitoes cannot enter the insectary. Measures include procedural (e.g.: restricted access, training, documentation, audits) and physical measures (e.g.: cages, climatic chambers, several doors from the outside, air and water filters) incorporated in the infrastructure of the facility. Only team members, who received a prior specific training, have access to the insectary (via badge or fingerprint entry). Visitors must be accompanied by an authorised member of the team at all times, and only after they have completed the visitor induction training.

There are several security features around the insectaries. Entering the insectary is a two-step process. The outer door can only be opened when the internal door is closed, and vice versa. Doors are fitted with powerful air curtains to prevent mosquitoes from flying through when the door is open. Furthermore, within the facility, mosquitoes are maintained with multiple levels of physical containment at all times, such as cages, which are within climatic chambers, isolated from the outside via at least two doors,

providing additional safeguards. It is important for the studies that we are conducting that we mimic the mosquitoes' natural habitat, to this end the insectary is kept at  $27\pm 2^{\circ}\text{C}$  and  $80\pm 10\%$  humidity. A computer records temperature and humidity so that we can ensure that the conditions are maintained. Any waste that is generated in the insectary is autoclaved before it is removed from the insectary, to ensure that all waste has been decontaminated, and sterilised before being disposed of.

All insectaries undergo inspection by national authorities and regulatory agencies to ensure they meet national requirements and that staff are adequately trained to work safely in the insectary before any research with modified mosquitoes takes place.

In addition, all of Target Malaria's insectaries are audited internally by the project to ensure they meet the project's internal standard of "facilities readiness"<sup>1</sup> before undertaking any project activity.

For more information about Target Malaria's insectaries:

[Target Malaria's Insectary in London at Imperial College London](#)

[Tour of Target Malaria's insectary at the MRTC in Mali](#)

[Tour of Target Malaria's insectary at the IRSS](#)

<sup>1</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5770120/>

