Part 1. RESEARCH PARTICIPANT INFORMATION SHEET

ResistAZM study:

An open label randomized controlled trial comparing the effect of ceftriaxone plus azithromycin versus ceftriaxone for the treatment of Neisseria gonorrhoeae on the resistome

Investigator:	Dr. Chris Kenyon
Sponsor:	Institute of Tropical Medicine (ITM), Antwerp, Belgium
Clinical site:	ITM HIV/STI clinic
Funder:	Institute of Tropical Medicine (ITM), Antwerp, Belgium

You are invited to take part in a research study which will be conducted in the HIV/STI clinic of the Institute of Tropical Medicine (ITM) and which seeks to contribute to preventing the emergence of resistance in gonorrhea and other bacteria.
Before you decide whether to participate or not in this study, it is important that you understand the information in this form, because it explains your rights, our responsibilities to you, the purpose, procedures, possible benefits, risks and inconveniences related to this study, and the right to refuse or stop your participation at any time.
Please, feel free to ask any questions at any time, for example about the possible benefits and possible risks related to this study. Your participation is completely voluntary. You can talk to anyone you trust about the research and you can take your time to think about whether you want to participate or not. In case you decide to participate, make sure you keep this background information and the signed consent form with you throughout the entire study period.

PURPOSE AND DESCRIPTION OF THE STUDY
Gonorrhea is a sexually transmitted infection (STI) which is caused by a bacteria (N. gonorrhoea) and which can manifest itself in the mouth/throat (pharyngeal gonorrhea), the rectum, or the genitals. This can occur with or without symptoms. Normally, any form of gonorrhea is treated with a single administration of antibiotics (ceftriaxone and azithromycin) and a check is performed after 14 days to see if the infection has disappeared.

There is a however a real possibility that gonorrhea may become untreatable with antibiotics in the near future. This is caused by resistance of the gonorrhea bacteria, which is a change over time of the bacterial characteristics which makes that the bacteria no longer respond to the antibiotics treatment. As a result, the infection is harder to treat and there is an increased risk of spreading of the diseases and severe illness.
This research study is done to better understand how gonorrhea is able to so rapidly develop resistance to antibiotics. In particular we want to see if gonorrhea is able to take up resistance mechanisms from other naturally occurring bacteria in your gut and in your mouth. When you get antibiotics this increases the amount of resistance genes in these bacteria that live in your gut, mouth

and elsewhere. We want to test if gonorrhea is able to use these resistance genes from the bacteria that naturally occur in your body to become resistant to antibiotics.

In this study, around 42 participants will take part in the ITM HIV/STI clinic in Belgium. Half of the participants will receive a treatment with a single antibiotic 'ceftriaxone' and the other half of the participants will be treated with a combination of 2 antibiotics: 'ceftriaxone' and 'azithromycin'. Participants will be randomly allocated into one of the 2 treatment groups. Both these treatments are approved by the Belgian regulatory authorities for the treatment of a gonorrhea infection and are widely used in routine practice. The main research question we will be testing is that treatment with 2 antibiotics results in more resistance than treatment with one antibiotic. If we find that 2 antibiotic therapy results in more resistance, then we will use this evidence to promote treatment with one antibiotic. Independent whether you will be treated with 1 or 2 antibiotics, you will receive a good treatment which is expected to cure your infection. Both the treatments with one or two antibiotics are close to 100% effective at eradicating gonorrhoea and both are recommended by national and international treatment guidelines.

HOW THE STUDY IS DONE

If you accept to be part of this study and if you meet the conditions to participate, you will be asked to attend 2 study specific visits (the current visit and a 2nd visit in 14 days), where the following procedures will be performed:

Visit 1 = Today Visit

The study doctor will ask you some standard medical questions (such as your antibiotic use in last year) as well as details on your lifestyle, including your sexual behavior.

As part of your standard treatment, we will take some samples from you today, in order to fully assess your gonorrhea infection. Some additional samples will also be taken for the purpose of this study:

- A urine sample
- An anal swab
- An oral rinse sample

You will then have the usual treatment for gonorrhea which is an injection of ceftriaxone 1g alone or in combination with 2g of oral azithromycin depending on the group you will randomly be assigned.

Visit 2 = Visit on day 14 (range day 13-15)

You will be asked to come back to this clinic after two weeks. This is a routine visit for all cases of gonorrhea and this visit is to check whether you have been cured. You will be asked some questions about how you have been, whether you have had any other health problems since having the treatment, about your sexual behavior, lifestyle and antibiotic consumption. If we diagnose any STIs these will be treated in the normal way.

We will then take the same additional samples as your first visit for the purpose of this study:

- A urine sample
- An anal swab
- An oral rinse sample

Know that you are also always welcome at ITM in between planned study visits in case of any questions, issues.

You will not have to pay for any of the treatment and procedures performed specifically for this study. You will not receive any compensation for study participation. Your transport costs, if any, will also not be reimbursed.

RISKS AND INCONVENIENCES
The risks related to this study for you are minimal. Participating in the study will mean that swabs are taken from your anus at both study visits; these swabs are however not invasive nor painful. Answering questions regarding your sexual behavior during study visits may be experienced as inconvenient.

BENEFITS
Your participation will give the scientific community an insight to the discovery of new ways to combat the resistance to antibiotics, which will likely become a major health problem in the near future.

INSURANCE
The organizer of this study, the Institute of Tropical Medicine, has obtained an insurance to cover any possible harm or injury that may be caused by participation in the study. If you get harmed or have questions about injuries as a result of being in the study, please contact the responsible researcher, Dr Chris Kenyon, 03 247 0786.

You can find more detailed information in Part 3.

STORAGE OF BODY SAMPLES
We would like to store your collected samples (urine, anal swab, oral rinse) for a maximum of 20 years after study completion to be used for future scientific research related to sexually transmitted infection. Such future studies will be separately approved by the Ethics Committee in advance and will not involve any genetic testing of your own human DNA.

You can indicate whether or not you agree with this future research in Part 2 of this document. Even if you decide that you do not want us to store your samples, you can still participate in the study.

You can find more detailed information in Part 3.

PRIVACY AND DATA PROTECTION
We will do everything we can to protect your privacy. Information about you will be treated as strictly confidential; it will be stored in an electronic database, and identified by a code and not by your name. The documents where your name is mentioned will not be shared with anyone, except the study researchers, your doctor and few other people who have to keep it confidential, such as specific employees of the Institute of Tropical Medicine.
All study data will be retained for a period of 20 years. The findings of the study will be published in (medical) journals. Your data can be shared with other researchers for future research, only upon condition that they are either pseudonymised (meaning that your name will be replaced by a code), or fully anonymized (meaning that the study code cannot be linked anymore to your name: nobody will know anymore that these data came from you).

Your name will not appear in any database, report or publication resulting from this study.

The study itself (and its results) will be published in the European public registry, http://www.clinicaltrialsregister.eu/, which is a public database of scientific studies with human participants. It does not contain any personal data of participants.

In accordance with the European Data Protection Regulation (GDPR), you may request access to and correct your personal data if needed.

You can find more detailed information in Part 3.

ETHICS COMMITTEE
Before the start, this study was reviewed and approved by the Institutional Review Board of the Institute of Tropical Medicine in Antwerp and an independent ethical committee appointed by the Belgian regulatory authorities. Any changes to the conduct of the study will also need to be approved by these ethical review boards before they are implemented.

VOLUNTARY PARTICIPATION
Your participation in this study is entirely voluntary. It is your choice whether you want to take part in it or not. Whether you choose to participate or not, all the services you receive at this clinic will remain the same.

You also have the right to stop your participation in the study at any time, even after you have signed this Informed Consent Form. You do not have to give a reason for stopping.
Also the researcher can decide to stop your participation in this study at any moment as well, without asking your permission, if he/she judges this in your best interest, or if it appears that you do not follow the requirements for participation. Should this happen, the researcher will explain this to you, and discuss what will happen afterwards.

CONTACT PERSON IN CASE OF QUESTIONS
If you have any questions concerning your participation in this study, your rights or if you think you have been harmed as a result of the study, please contact, now, during, or after the study:

Chris Kenyon
Institute of Tropical Medicine
Antwerp
Tel 03 247 0786 (After hours: 03 821 3000. Ask for the Infectious Diseases doctor on-call)
ckenyon@itg.be

Part 2. INFORMED CONSENT FORM

CONFIDENTIAL

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To be completed by the participant

I have received a copy of the written participant information sheet (part 1). I also received verbally sufficient and understandable explanations, with enough time to ask questions, and my questions were satisfactorily answered.
I freely consent to participate in this study and to cooperate in the study examinations/activities.
I understand that during the study, my personal and medical data will be recorded, and that the confidentiality of this data will be protected according to the applicable laws in Europe and Belgium.

☐ Yes / ☐ No: I agree that samples collected for the study are stored for a maximum of 20 years after completion of this study and may be used for future scientific research related to sexually transmitted infections (not including human genetic testing).

Date: __ __ / __ __ / __ __ __ __

Name of participant: _____

Signature of participant: _____

To be completed by the research staff obtaining the informed consent

I, undersigned, _____ confirm that I have informed the participant about all the relevant aspects of this study. I confirm that he has consented voluntarily to participate in the study.

Date: __ __ / __ __ / __ __ __ __

Signature: _____

Part 3. ADDITIONAL INFORMATION

ResistAZM study:

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1. Insurance

Any participation in a study involves a risk, however small it is. The sponsor is, even if there is no fault, responsible for damage caused to the participant (or in the event of death, his/her dependents) and directly or indirectly caused by his/her participation in the study. The sponsor has taken out insurance for this responsibility.

You are therefore asked to report any new health problem to the investigator. He/she will be able to provide you with additional information concerning possible treatments.

The insurance does not cover the natural progression of disease or known side effects of your normal treatment. If the investigator believes that a causal link between a new (health) complaint and your participation in the study is possible, he/she will inform the study sponsor, which will initiate the declaration procedure to the insurance company. The latter will appoint an expert - if considered necessary - to assess whether there is a link between your new health problems and the study.

In the event of disagreement either with the investigator or with the expert appointed by the insurance company and also whenever you feel it is appropriate, you or - in case of death - your dependents may bring proceedings against the insurer directly in Belgium (AMLIN Insurance SE, B-1030 Brussels, Koning Albert II-laan 37).

The law provides that the insurer may be summoned to appear either before the judge of the location where the event giving rise to the damage occurred, or before the judge of your domicile, or before the judge of the insurer's registered offices.

2. What happens with your samples collected during the study

Your biological samples collected for the purpose of the study are pseudonymised (i.e. your identity will be replaced by an ID code in the study) and thus they carry an identification code and not your name.

The Biobank Manager for the samples at the Institute of Tropical Medicine (Dr. Maartje Van Frankenhuijsen, Department of Clinical Sciences) undertakes to ensure that they will be used within the context of clinical research and destroyed at the end of the scheduled storage period.

If you withdraw your consent to take part in the study, you can also ask to have your samples destroyed. Contact the investigator or biobank@itg.be if you want to do so. The test results obtained from your samples before you withdraw your consent will however be retained by the study sponsor.

Your samples will not be used for human genetic testing. Your samples will also not be sold to commercial companies.

Possibly, your samples are interesting for future research which explains why they are preferably stored for a longer period. To allow such a long term storage, your additional consent is requested in Part 2 of this document. This research will be in the same research domain or research about the same disease as in this study. It will also have to be approved by an Ethics Committee. Even if you agree with this secondary use of your samples, you have the right to have your samples destroyed at any later moment. You also have the right to have your stored samples anonymized[1] at any moment. The long-term storage and management of your samples always happens as described by the law[2].

The biological material collected within the study are considered as a "donation" and you should be aware that, in principle you will not receive any financial benefit (royalties) associated with the scientific research or the development of new diagnostics/therapies derived from the use of your donated samples.

3. Data protection and rights of participants in the study

Your participation in the study means that you agree that the investigator collects and records your personal and medical data, and that the study sponsor (that is the research institute that organized and conducts the study) uses them for research purposes and in connection with scientific and medical publications.

Your data will be processed in accordance with the European General Data Protection Regulation (GDPR) and with the Belgian legislation on the protection of natural persons with regard to the processing of personal data. The sponsor of this study, that is Institute of Tropical Medicine, acts as data controller for your data and the lawful ground for the data processing is the public interest.

You are entitled to ask the investigator what data are collected about you and how they are used for the study[3]. This data may concern your current (clinical) situation but also some of your demographic data, lifestyle data, (medical) background, the results of previous medical examinations , and obviously the results of examinations required by this protocol.

[1] Meaning that the link to your identifying information like your name is completely broken and thus cannot be traced back to you.

[2] Law on human body material of 2008 and the Royal Decree on biobanks of 2018.

[3] These rights are guaranteed by the European Data Protection Regulation 2016/679 (GDPR), the Belgian law on the protection of natural persons with regard to the processing of personal data of 30 July 2018 and the Law of 22 August 2002 on patient rights.

In case you wish to withdraw your consent for participation, the pseudonymised data that was collected about you before your withdrawal will be retained. This is to guarantee the validity of the research.

The investigator has a duty of confidentiality with regard to the data collected.

This means that he/she commits to never reveal your name in the context of a publication or conference, but also that he/she commits to pseudonymize your data, before they are recorded and processed for analysis. The investigator and his/her team will therefore be the only ones to be able to establish a link between the data recorded and analysed in the study and your name or medical records.

Care will be taken not to transmit data that contain any combination of elements that might allow you to be identified[4].

To verify the quality of the study, it is possible that your study data will be examined by persons subject to professional secrecy and designated by sponsor of the study, the national regulatory authority, or an independent audit body. In any event, this examination of your records may only take place under the responsibility of the investigator (or one of the collaborators designated by him/her).

The sponsor will use the data collected within the context of the study in which you are taking part, but would also like to enable use of the data for future research in the same research context as this study. Any use of your data outside the context described in this document is only possible with the approval of an ethics committee and ITM's data access committee.

For future studies, your pseudonymised or anonymized data could also be transferred to countries outside Belgium and Europe where the standards about data protection may be different or less stringent. In such a case, the sponsor will assure that appropriate warranties are present with regard to the transfer and later use of the data in a secure and correct way.

If you have any questions relating to how your data are being processed, you may contact the investigator. Also the data protection officer of ITM can be contacted (email: informatieveiligheid@itg.be or tel. 03 247 07 43).

Finally, if you have a complaint concerning the processing of your data, you can contact the Belgian supervisory authority who ensures that privacy is respected when personal data are processed.

Data Protection Authority (DPA)
Drukpersstraat 35,
1000 Brussels
Tel. +32 2 274 48 00
e-mail: contact@apd-gba.be
Website: https://www.dataprotectionauthority.be

[4] The database containing the results of the study will therefore not contain any combination of elements such as your initials, your gender and your full date of birth (dd/mm/yyyy).