

INSTRUCTION SHEET: ENGLISH VERSION

For any further queries, please contact the persons listed at the end of the study information sheet (page 5)

Your kit (= 1 plastic bag) contains:

- One copy of this instruction sheet.
 - One copy of the study information sheet together with the consent form(s) with your participation code.
 - Two containers (one blue and one white), both with your participation code (i.e., study code).
 - One letter with the IFIK logo and your study code.
 - One white envelope with your study code.
-
1. Read the study information document. Then, if you wish participate in this study, sign the consent form(s).
 2. Open the blue container: collect the stools with the spatula and transfer them to the same container. Important: a good amount of stools should be introduced in the container (see figure in the back of this sheet).
 3. Close the blue container and place it inside the white one. Then, place the white container in the white envelop. Important: store the envelope in the refrigerator (4-5°C) until final shipment to the IFIK in Bern.
 4. The signed written consent(s) must be enclosed inside the letter with the IFIK logo and sealed afterwards.
 5. The letter and the white envelope can be sent by ordinary post to the IFIK in Bern. Note that both are prepaid.

u^b **SI-XXX-YY**

Study Information
Patient consent form
Consent for further use
English Version

IFIK INSTITUT FÜR
INFEKTIONSKRANKHEITEN

**Molecular Features of Multidrug-R^r
Swiss Embassy B^r**

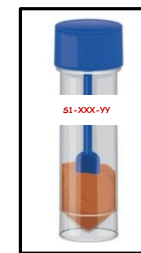
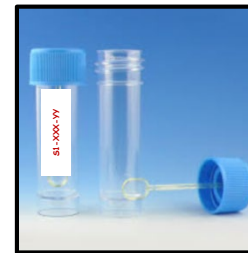
This project is organized by the Inst^r
iversity of Bern.

Dear Madam, dear^r
We like to follow^r
overview.

Summary

1	Goal of the research: The research aims to identify the proportion of Swiss embassy employees and their relatives and MDR Enterob. with multidrug-resistant Gram-negative bacteria (broadly characterized MDR Enterob.) in their gastrointestinal tract. The project also aims to characterize the strains of identified bacteria.
2	Selection of study participants: You are working for the Swiss embassy (or you are a relative or a partner from a Swiss embassy employee) in a country outside of Switzerland. This is the reason why we are sending you this study information.

Read and Sign



With the spatula collect your stools and place them in the blue container.

Close the blue container (with the stools) and place it inside the white one.

Read the study information sheet and sign the consent form(s)



Place your signed consent(s) inside this letter. Seal the letter tightly. Only a few study team members will see the uncoded data (see section 10 of the study information sheet)



Put the white container inside this envelope. Seal it tightly and store in a refrigerator at 4-5 °C until ready for shipment.

Send both letter and white envelop to the IFIK in Bern using the ordinary post service



IFIK, Bern

Molecular Features of Multidrug-Resistant Enterobacterales Colonizing Swiss Expatriates

This project is organized by the Institute for Infectious Diseases (IFIK) of the University of Bern.

Dear Madam, dear Sir

We would like to ask whether you are willing to voluntarily participate in our research project. On the following pages, we present the research project. First, you will find a summary to give you an overview. A detailed description is then presented.

Summary

1	<p>Goal of the project: Our aim in this research project is to investigate the proportion of Swiss expatriates (and their relatives and partners living in the same household) who are colonized in their gastrointestinal tract with bacteria resistant to numerous antibiotics (termed multidrug-resistant Enterobacterales [MDR-Ent]). We also aim to characterize molecular patterns in the identified bacteria.</p>
2	<p>Selection of study participants: You are living in a country outside of Switzerland. This is why we are sending you this study information.</p>
3	<p>General information about the project: The aim of this project is to identify risk factors for MDR-Ent intestinal colonization. The results of the study will have key implications for possible countermeasures that may be applied to prevent the acquisition and transmission of these bacteria to other individuals (e.g., educational program to improve hygiene). The information on different molecular features of MDR-Ent will provide important insights regarding the clones that could be imported to Switzerland in the near future. The data will be essential for designing novel therapeutic and diagnostic strategies for our health-care systems.</p>
4	<p>Course of the project/study procedures: This is a cross-sectional study. This means that we are conducting an investigation 'once across the study populations'. We are asking you to fill out a questionnaire and to donate stool after having read this study information. No additional investigations are required for this study. We anticipate having data and stool samples from all study participants around the world within 12 months. We anticipate that all analyses will be conducted within 3 years.</p>
5	<p>Benefit: There is no direct benefit for you. There are indirect benefits in knowledge transfer.</p>
6	<p>Rights: You decide voluntarily whether or not you wish to participate in the study. Your decision has no influence on your medical care or your occupation, and you do not have to justify your decision.</p>
7	<p>Duties: Your participation requires completion of the consent document provided and the questionnaire, as well as a stool donation.</p>
8	<p>Risks: The study holds no risk for you.</p>

9	Results: If you wish to be informed about the study results, kindly indicate your email address. Should we unintentionally identify results concerning a disease, you will be actively informed.
10	Confidentiality of data and samples: We will collect your health-related data and a stool sample. All data and samples will be coded. We are obliged to follow all Swiss rules and regulations on data protection. All members of the study team must follow confidentiality rules.
11	Withdrawal and discontinuation: You can withdraw from the project at any time. The data and samples obtained <i>prior</i> to the time of your withdrawal will be analyzed.
12	Financial compensation: No compensation or payments will be given to the project participants.
13	Liability: Because this study holds no risk, no insurance is required (Art 2.b KlinV; Art 13 HFV). IFIK of the University of Bern is liable in the event of project-related damage or injuries.
14	Funding of the project: This project will be supported by the Swiss National Science Foundation (SNF; grant No. 32003B_184726 to A. Endimiani).
15	Contact information: Please do not hesitate to contact the persons listed at the end of this study information should you have any questions.

Detailed Information

1. Goal of the project

Our aim in this research project is to investigate the proportion of Swiss expatriates (and their relatives or partners living in the same household) who are colonized with antibiotic-resistant Gram-negative bacteria (termed multidrug-resistant Enterobacterales [MDR-Ent]) in their gastrointestinal tract. We also aim to characterize molecular patterns in the identified bacteria.

2. Selection of study participants

You are living in a country outside of Switzerland. For this study, we are contacting Swiss people around the world, and hence, this is why we are sending you this study information. You can participate in the study if you are ≥ 18 years old and are a Swiss citizen. If you are a relative or a partner of a Swiss expatriate living in her or his household, you are also welcome to participate. However, the study requires participants to have lived or worked for at least 3 months in the foreign country.

3. General information about the project

Background: Enterobacterales (Ent) are an order of Gram-negative bacteria that are frequently responsible for infections in humans. For instance, *Escherichia coli* is the most frequent pathogen causing urinary tract and bloodstream infections. Usually, antibiotic treatment of such infections is easy and guarantees a complete resolution of the infection. However, in the last 20 years, we have observed a drastic increase of bacteria that are resistant to commonly used antibiotics. These pathogens are therefore defined as “multidrug-resistant (MDR) bacteria”.

MDR-Ent can be found in the intestinal tract of healthy people. Notably, colonization is not harmful and does not mean you have an infection, but it can contribute to the spread and transmission of MDR-Ent. Unfortunately, it is not clear how healthy people acquire such bacteria. Few surveys have explored lifestyle factors (e.g., diet) and behaviors (e.g., living in other countries) associated with intestinal colonization.

Geographic areas of the project: This is a 'national' project because it focuses only on Swiss citizens and their relatives and partners. However, from a geographic point of view, it is an international project because it involves Swiss people living around the world.

Study design: This is a cross-sectional study. This means that we are conducting an investigation once across the study populations.

Duration of the project: We anticipate having data and stool samples from all study participants around the world within 12 months. The detailed analysis of data and bacteria will take longer. We anticipate demonstrating the final study results within 3 years.

Number of study participants: Overall, we anticipate 750 study participants.

Human Research Act: We are obliged to follow all Swiss rules and regulations on data protection. All members of the study team must follow confidentiality rules.

4. Course of the project/study procedures

We are asking you to fill out a questionnaire and to donate stool after having read this study information. After analyzing your stool sample, we will be able to know:

- 1) the percentage of healthy Swiss people living in foreign countries who are colonized at the intestinal level with MDR-Ent; and
- 2) the molecular characteristics of such bacterial pathogens.

Using the data obtained from your questionnaire, we will be able to identify the risk factors favoring intestinal colonization. Knowledge of these conditions will help to explain the consistent rise of these bacteria and can help with the development of new interventions (e.g., strategies to prevent colonization or approaches to decolonize people) and educational programs to limit the spread of these bacterial pathogens.

This study information is accompanied by instructions on how to collect and ship the stool sample. You can participate in the study only if the questionnaire is filled out and the stool sample is shipped. No additional investigations are required for this study. It is possible that we will contact you for a follow-up study. A follow-up study must also be reviewed and approved by the Ethical Committee and follow Swiss rules and regulations. If you do not wish to be contacted for a follow-up study, kindly indicate this in the questionnaire.

5. Benefit

No compensation or payments will be given to you, but there are indirect benefits in knowledge transfer. The study results may help others and can help implementing more adequate antibiotic treatments in case of infection (e.g., urinary tract infection) and set strategies to prevent transmission (e.g., in the household).

6. Rights

You decide voluntarily whether or not to participate in the study. Your decision has no influence on your medical care or your occupation, and you do not have to justify your decision. You can withdraw from the project (withdrawal of informed consent) at any time (see below, "11. Withdrawal and discontinuation").

7. Duties

Your participation requires completion of the consent documents provided and the questionnaire, as well as a stool donation.

8. Risks

The study holds no risk (interventional or medical) for you because you only have to donate stool.

9. Results

If you wish to be informed about the study results, kindly indicate your email address. Should we unintentionally identify results concerning a disease, you will be actively informed.

10. Confidentiality of data and stool samples

We will collect health-related data and a stool sample. The purpose of sampling stool is to identify MDR-Ent. Only a few study team members will see uncoded data, and only when they have to fulfil defined tasks in the study project. However, as you may have noticed with the code labels accompanying this study information, data will be obtained in coded form from the beginning of the study. Thus, data that could identify you (e.g., name, birth year) will not be visible to anyone outside of the study team. Moreover, study team members require a username and password to access core data, and we are able to track every single access. Thus, project data will be handled with the utmost discretion and are accessible only to authorized personnel who require the data to fulfil their duties within the scope of the research project.

The summarized data will be presented in a scientific publication, and it is impossible to track you as an individual from a scientific publication. Your name will never appear on the Internet or in a publication. In selected circumstances, journals request submission of "raw" data. However, even then, only coded data will be submitted, which does not allow any connection to an individual person. Data and stool samples will be stored in databanks and biobanks at the campus of the University of Bern, Bern, Switzerland, for research purposes only. It is possible that we will use the material for further studies in future. Therefore, we have added 2 consent forms to this study information, one for this study and one for 'further use'.

It is possible that the project will be audited by the responsible Ethical Committee. During an audit, the ethical committee may ask to review personal and medical data for control purposes. However, all individuals working for the Ethical Committee must follow rules and regulations on confidentiality.

11. Withdrawal and discontinuation

You can withdraw from the project at any time. The data and samples obtained *prior* to the time of your withdrawal will be analyzed. If you wish to withdraw, kindly indicate your withdrawal by contacting the person listed at the end of this document. If withdrawal is communicated during the project, data from the questionnaire and stool and bacterial strains will be used in coded form until the study is terminated. Otherwise, the project would lose its scientific value.

After study termination, assigned codes will be completely and irreversibly anonymized. That means that no one can track the person that the data is derived from. Data and isolated bacteria will be kept with an anonymized number, and the stool sample will be destroyed. If study withdrawal is communicated *after* project termination, the aforementioned process will be conducted immediately.

12. Financial compensation

No compensation or payments will be given to the project participants. No costs will be a burden to your health insurance or to you. All project-related costs will be covered by the primary investigators and their affiliations.

13. Liability

Because this study consists of no investigation risk (stool samples), no insurance is required (Art 2.b KlinV; Art 13 HFV). In the event of project-related damage or injuries, IFIK of the University of Bern is liable, except for claims that arise from misconduct or gross negligence. The process will follow the rules and regulations stated in Swiss law. Kindly contact the persons listed below should you experience project-related damage or injury.

14. Funding of the project

Project-related costs will be completely covered by the primary investigators and their affiliated institutions. This project is supported by the Swiss National Science Foundation (Grant No. 32003B_184726).

15. Contact information

Please do not hesitate to contact the persons listed below should you have any questions. Because Swiss Expatriates are located all around the world, we are happy to offer electronic means for communication (i.e.; Skype, Zoom, FaceTime, WhatsApp). Kindly contact us via email first, and we will get in touch with you.

Prof. Dr. med. Andrea Endimiani, PhD, FISAC
Languages: Italian, English
Email: andrea.endimiani@ifik.unibe.ch
Phone number: +41 31 632 86 32

or

Prof. Dr. med. Parham Sendi, FIDSA
Languages: German, French, English
Email: parham.sendi@ifik.unibe.ch
Phone number: +41 31 632 69 86

Address and fax number:

University of Bern
Institute for Infectious Diseases (IFIK)
Friedbühlstrasse 51,
CH-3001 Bern,
Switzerland
Phone number for contact center: +41 31 632 32 65
Fax: +41 31 632 87 66

Consent Declarations

Written consent declaration to participate in the study project: Kindly read this form carefully. Please ask if there is anything that you do not understand or if you require more information.

BASEC number:	2020-01683
Title of the project:	Molecular Features of Multidrug-Resistant Enterobacterales Colonizing Swiss Expatriates
Responsible Institution:	University of Bern, Institute for Infectious Diseases (IFIK)
Location of study conduction:	University of Bern, Institute for Infectious Diseases (IFIK)
Project leaders:	Andrea Endimiani, Parham Sendi
Study participant: First and last name in print: Date of birth:	 <input type="checkbox"/> Female <input type="checkbox"/> Male

- I was well informed via this study information about the content, the course, the benefits, and the risks of the study.
- I am participating in the project voluntarily, and I accept the content of the study information. I had sufficient time to make my decision.
- I had opportunities to ask questions, and questions about the study were answered.
- I can keep the study information document, and I will receive a copy of my consent declaration.
- I consent that members of the Ethical Committee may review my uncoded data during an audit, provided that strict confidentiality is guaranteed.
- If study results or random findings concern my health, I will be informed. If I do not wish to be informed, I will let the primary investigators know.
- I can withdraw from the project at any time without any justification, and my decision has no influence on my medical care or my occupation. The data and samples obtained *prior* to the time of my withdrawal will be analyzed.
- In the event of project-related damage or injuries, IFIK of the University of Bern is liable.

Place, Date	Signature of study participant

Confirmation of the project leaders: We hereby confirm that the purpose, the course, and the consequences of the study were explained to the study participants via the study information sheet. We confirm that all project-related duties will be fulfilled according to the applicable law. Should we realize during the study period that there are aspects that could potentially influence the consent decision of the study participant, she/he will be immediately informed.

Place, Date	First and last name in print, and signature of project leader

Consent declaration for further use of health-related data and stool samples in coded form

BASEC number:	2020-01683
Title of the project:	Molecular Features of Multidrug-Resistant Enterobacterales Colonizing Swiss Expatriates
Responsible Institution:	University of Bern, Institute for Infectious Diseases (IFIK)
Location of study conduction:	University of Bern, Institute for Infectious Diseases (IFIK)
Project leaders:	Andrea Endimiani, Parham Sendi
Study participant: First and last name in print: Date of birth:	 <input type="checkbox"/> Female <input type="checkbox"/> Male

I hereby consent that my data and samples used in the projects may be used in coded form for further biomedical research. My data and samples will be stored in a databank and biobank for a further – not yet defined – research project for an unlimited time. The consent is not limited.

My decision is voluntary, and I can withdraw this decision at any time. If I withdraw my decision, the data will be anonymized and the stool samples destroyed. I will inform the project leaders and do not have to justify my decision.

I understand that my data and samples are coded, and the key to this code is kept securely. Data and samples may be sent for analysis to other institutions and biobanks in Switzerland and abroad, provided that they fulfill the same standard precautions as required in Switzerland. All legal aspects regarding data confidentiality will be followed.

Generally, all data and samples will be analyzed together and not separately, and the study results, including all data, will be published. In the case of a single result that is of concern or relevance for my health, the project leaders will contact me. If I do not wish to be contacted, I will notify the project leaders.

In the case that the study results derived from the data and samples are commercialized, I will have no claim on the commercial application.

Place, Date	Signature of study participant

Confirmation of the project leaders: We hereby confirm that the purpose, the course, and the consequences of the further use of these data and samples were explained to the study participants via the study information sheet.

Place, Date	First and last name in print, and signature of project leader

1. FIRST NAME: _____ LAST NAME: _____

2. Year of birth: _____ 3. Gender: Male Female

4. Personal email address: _____

5. When did you collect your stools? _____ Date (day/month/year): _____

6. Where do you live? _____ Country: _____ City: _____

7. Do you work for a Swiss Embassy?
 Yes No No, but I am a relative/partner of an embassy employee

8. Including yourself, what is the number of people that live in your foreign household? _____

9. What are their ages (e.g., 10, 43, 48)? (excluding yourself) #1 #2 #3

10. Is any of them a participant in this study? Yes [please add below their study code(s)] No
STUDY CODE(S): #1 #2 #3

11. Since when have you been living in the current foreign city? _____ Date (month/year): _____

12. Have you lived in other countries in the last 5 years? Yes (add below where and when: months/years) No
#1: #2:
#3: #4:
More: _____

13. Do you plan to return again to Switzerland for holidays in the next year? Yes (approx. when?): _____ No

14. Where do you usually stay when you return to Switzerland?
 I am a guest of relatives I am a guest of friends Own home Other

15. Did you visit other countries for >2 days in the last year? Yes (add below where and approx. when) No
#1: #2:
#3: #4:
More: _____

16. Any hospitalization(s) during the last 2 years? Yes (please add below where and approximately when) No
#1: #2: _____

17. Did you take any antibiotic during the last year? Yes (please add below approximately when) No
#1: #2: #3:
More: _____

18. Do you have any chronic disease(s) affecting the gastro-intestinal tract? Yes No

19. Are you constantly taking stomach antacids or acid reducers? Yes No

20. Have you experienced diarrhea in the last 3 months? Yes No

21. What kind of diet do you usually follow?
 Omnivore Rawist Vegetarian Vegan

22. How many times per week do you usually eat raw meat (not cooked)?
 0 (zero) 1 2 3-6 ≥7

23. How many times per week do you usually eat raw fish (not cooked)?
 0 (zero) 1 2 3-6 ≥7

24. How many times per day do you usually eat a portion of fresh vegetables and/or fresh fruit?
 0 (zero) 1 2 3 ≥4

25. How many times per day do you usually eat a portion of fresh cheese and/or dairy products (e.g., yogurt)?
 0 (zero) 1 2 3 ≥4

26. Do you regularly drink milk (i.e., ≥1 glass/day)? Yes No

27. Do you regularly drink tap water? Yes No

28. How many beers (pints of ~0.5 l) do you drink per week? 0 1-7 8-14 >14

29. How many glasses of wine do you drink per week? 0 1-7 8-14 >14

30. How many times per week do you usually have breakfast outside your foreign home?

31. How many times per week do you usually have lunch outside your foreign home?

32. How many times per week do you usually have dinner outside your foreign home?

33. Do you have pets in your foreign home? Yes (add below animal and age; e.g., #1: dog, 3 year-old) No
#1: #2: #3 or more:

34. Have any of the above pet(s) been hospitalized for >1 day and/or treated with antibiotics in the last year?
 Yes (please indicate the # used in question 32) No

35. Do you have any contact with other animals (e.g., pigs, cows, horses) during the week?
 Yes [please add which animal(s)] No

36. Do you practice outdoor sports/hobbies in close contact with nature (e.g., jogging, fishing, hunting)?
 Yes (which?) No

37. Would you be interested in a follow-up study similar to this one? Yes No
