Study information on SEMVAc

Safety and **E**ffectiveness of **MVA**-BN Va**c**cination against MPXV Infection
in at-risk individuals in Germany

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Study Center: **Dr. med. Axel Baumgarten**
zibp – Zentrum für Infektiologie Berlin Prenzlauer Berg GmbH
Driesener-Str. 20/23
10439 Berlin

Dear Mr./Ms.,

we would like to offer you the opportunity to participate in a scientific study investigating the safety and effectiveness of the MVA-BN vaccine (Imvanex® by Bavarian Nordic) against monkeypox infection (Monkeypox virus, MPXV).

The study includes both people who receive a vaccination and people who do not receive a vaccination. Vaccination is carried out as part of the clinical routine and independently of the study. Whether you receive a vaccination is not affected by study participation. If you participate in the study and initially do not receive a vaccination, you can choose to receive a vaccination at a later time and still remain a study participant (switching from the group of unvaccinated to the group of vaccinated individuals is possible).

If, in the course of the study, you receive a vaccination as a post-exposure prophylaxis (vaccination after you have had contact with a known case of monkeypox in order to prevent the onset of the disease or mitigate its course) your study participation is automatically terminated as the investigation of post-exposure prophylaxis is not part of this study.

In total, the study is carried out throughout Germany with up to 20,000 people who are classified as a risk group. Regular short surveys are sent to participants via e-mail. In a subgroup of participants (up to 2,000 people) a small amount of additional blood, at most 10ml per visit (less than one tablespoon of blood), is taken during routine blood collection and will be tested for antibodies.

Before you decide to participate in this study, it is important for you to carefully read and understand the following information.

Your participation in this study is voluntary. You will only be included in this study if you give your written consent. If you do not want to participate in the study or want to terminate your participation at a later time you will not experience any disadvantages.

The following text is intended to explain the study objectives and procedures and to provide you with specific information on data protection and biomaterials (if applicable). Please do not hesitate to address any points that are unclear to you. You are welcome to mark sentences/sections that you did not understand to discuss. You will then be given sufficient time to think about your participation.

BACKGROUND OF THE STUDY

Monkeypox is a rare disease first detected in West and Central Africa in the 1970s and occurs primarily in animals, probably mainly in rodents. It is caused by the monkeypox virus (MPXV).

The infection is transmitted through direct skin or mucosal contact, possibly also via droplets. According to the current state of knowledge, most patients do not become seriously ill but may experience painful skin lesions and scarring.

The first outbreak outside Africa took place in 2003 with around 70 cases in the US and was likely related to infected prairie dogs. In 2017, Nigeria experienced the last major outbreak with 500 suspected and 200 confirmed cases. Since then, only isolated cases have been reported.

The current outbreak differs significantly from previous outbreaks in several aspects, raising a number of questions regarding the development of the disease, infectiousness, clinical symptoms, and immune response. Thus, an adaptation of the virus seems possible, leading to increased infection rates and a faster spread. The occurrence in different unrelated clusters and without a comprehensible chain of infection is remarkable since barely symptomatic or totally asymptomatic transmission seems possible.

AIM OF THE STUDY

The *Modified Vaccinia Ankara* vaccine manufactured by Bavarian Nordic (MVA-BN) is approved for the prevention of smallpox infections in the EU, and in the US also against MPXV. Due to high structural similarity a high efficacy against MPXV can also be assumed and the European Medicines Agency (EMA) has authorized the vaccine under "exceptional circumstances". However, so far only animal data on the efficacy of MVA-BN against MPXV is available. In its announcement of 21.6.2022, the Standing Committee on Vaccination in Germany (STIKO) recommends the (off-label) use of MVA-BN as a post-exposure prophylaxis after monkeypox exposure and as a vaccination for persons with an increased risk of exposure (risk of encountering a pathogen/source of infection) and/or risk of infection (risk of becoming infected during such contact).

The aim of this study is to assess the safety and efficacy of MVA-BN as part of the national vaccination campaign, thus contributing valuable data to the epidemiological management of monkeypox. In addition, information on immune responses will be investigated by means of antibody analyses.

INFORMATION ON STUDY PROCEDURES

The duration of your study participation is about 12 months. The study ends on 31.12.2023, individuals may therefore be enrolled until 31.12.2022. If you decide to participate in this study, you will receive a questionnaire on the day of inclusion (electronic or paper-based) gathering baseline information (e.g., age, gender, pre-existing medical conditions) and infection risks including sexual history. We ask you to complete this questionnaire on your own. Filling in takes about 5 to 10 minutes at most. During the duration of your study participation, you will receive a short monthly questionnaire (maximum 2-5 minutes for completion) by e-mail, in which any symptoms and exposure risks will be recorded. If you

receive one or two doses of MVA-BN vaccine, you will be asked about possible symptoms and tolerability 2 weeks after each vaccination.

In a subgroup of study participants (about 2,000 people), a small amount of additional blood (maximum 10ml) will be drawn during quarterly routine blood examinations as indicated by your physician. Thus, no additional venipuncture will be performed for the study. The blood is then processed in the laboratory and used for antibody measurements. Please indicate in the consent form whether you agree to this blood analysis.

If you develop symptoms of monkeypox infection during the study period or have had contact with a person infected with monkeypox, please contact your study center to inform your physician. This also applies if you have received a monkeypox vaccination somewhere other than your study center. In case of vaccination as a post-exposure prophylaxis your study participation is automatically terminated, as the investigation of post-exposure prophylaxis is not part of this study.

		Time (W=week)				
Group	**Measure**	**W0**	**W2**	**W4**	**W6**	**up to 1 year**
no vaccination, without blood sampling	Study Visit for Inclusion	x				
	Questionnaire	x		x		Monthly, of which once a quarter as part of the routine treatment with your treating physician
no vaccination, with blood sampling	Additional to above serology	x				Quarterly as part of routine treatment with your treating physician
Vaccination without blood collection	Study Visit for Inclusion	x				
	1. MVA-BN vaccination*	x				
	2. MVA-BN vaccination*			x		
	Questionnaire	x	x	x	x	Monthly, of which once a quarter as part of the routine treatment of your treating physician
Vaccination with blood sampling	Additional to above serology	x		x		Once a quarter as part of routine treatment with your treating physician
* Vaccination with MVA-BN is independent of the study.						

RISKS AND BURDENS OF PARTICIPATION IN THE SEMVAC STUDY

Possible burdens are usually limited to filling out questionnaires, some of which include intimate questions about your sexual and risk behavior. Your answers in the questionnaires cannot be traced back to you by the study team.

In a subgroup of participants, a small amount of additional blood (max. 10ml) is taken during routine blood collection. This does not pose any additional risks for you.

In order to send the electronic surveys it is necessary that your e-mail address is passed on to the principal investigators' team. Depending on your e-mail address it could be possible to identify you. The persons involved are obliged to maintain confidentiality.

POSSIBLE BENEFITS FOR YOU

You do not benefit directly from participating in this study. However, the expected findings of the study can lead to a considerable group benefit through a better understanding of the MVA-BN vaccine and thus individual treatment options and possible prevention measures against monkeypox infection. As a result, an individual risk of infection can also be better estimated.

EXPENSE ALLOWANCE

For your participation in the SEMVAc study you will be granted an expense allowance of 30€ for the inclusion visit and 20€ per study visit at your study site, in total up to 130€. For participants in the subgroup with additional blood analyses an additional expense allowance of 10€ per blood collection will be granted.

INFORMATION ON DATA PROTECTION

a) General information

During the study, medical findings (health data, etc.) as well as personal information (such as age, gender, etc.) are collected from you for a specific purpose and written down in your personal file at the study center or stored electronically. The data relevant to the study is also stored in pseudonymized (encrypted) form.

Pseudonymized means that no information with which you can be directly identified (e.g., name, contact information, date of birth, etc.) is used, but only a number and/or letter code. In your study center, a pseudonymization list is created that is protected against unauthorized access. This is necessary to trace personal data back to you, if necessary. This de-pseudonymization only occurs to legally permissible extent. However, it can never be completely ruled out that conclusions could be drawn about your person even without this list.

b) Legal basis

The legal basis for data processing is your informed consent in accordance with Article 6(1)(a) and Article 9(2)(a) of the EU General Data Protection Regulation (GDPR).

The provision of your personal data is voluntary and freely revocable. However, you cannot participate in this study without your expressed consent to the processing of your data.

c) Accountability

The principal investigator and your study center are responsible within the means of the data protection law. Your study center remains responsible for your identifying treatment data.

d) Purpose(s)

With the help of the collected data, the safety and effectiveness as well as immunogenicity (i.e., the triggering of immune responses) of the MVA-BN vaccine will be investigated.

During the study and afterwards, new findings regarding the immune responses against MVA-BN may emerge or new measurement methods may be developed that allow a more detailed capture of the immune response. Therefore, some of the blood samples are stored in a biobank to be analyzed at a later date. In addition, in the course of the study it may occur that conspicuous immune responses are detected in a subgroup of study participants, which can be determined in more detail with additional examinations. The data and samples can be reused for additional investigations, so if new findings or new methodologies for measuring immune responses emerge in the course of the vaccination campaign or beyond, existing data and samples can be further examined by the scientists involved in the study. This can also occur after the study has been completed and serves as an additional insight into the effect of MVA-BN and immunity to MPXV. That way, the knowledge gained from the study can be further increased. The same confidentiality and data protection requirements apply without restriction. However, the prerequisite for the use of the biomaterials and data for a later medical research project is that the research project has been evaluated by an ethics committee and that you have given your consent. We ask you to indicate in the declaration of consent whether your samples may be used a) for other vaccine research and b) for other research purposes.

e) Transfer/Recipient

The data and biomaterials relevant to the study are additionally processed in pseudonymized form and, if necessary, passed on.

The pseudonymized data and biomaterials collected from you will, if necessary, be passed on to:

1. *Study director at the Charité – Universitätsmedizin Berlin* and bodies commissioned by them for the purpose of implementation and scientific evaluation,
2. laboratories of the Charité – Universitätsmedizin Berlin and the University Hospital Cologne involved in this study,
3. to the commissioned biobank of your study center,
4. to the Robert Koch Institute, Department of Vaccination Prevention (Seestraße 10, 13353 Berlin) (only pseudonymized data for epidemiological investigations).

Your data that is collected and stored as part of the study (including the original clear data) can be viewed as far as necessary by representatives of the study management (so-called monitors) to check the proper execution of the study in your study center. These are obliged to confidentiality; a transfer of the collected data does not take place in this context. To this end, you release your study physicians from confidentiality.

In addition, your e-mail address is passed on to the team of the principal investigator to send the study-specific questionnaires.

f) Your rights

In principle, you have the following rights with regard to your personal data, unless this is technically or otherwise legally impossible due to the deletion of the identifying features for decryption in the meantime:

Right to withdraw your consent

You can revoke your consent to the processing of the collected data and/or analysis of your biomaterials at any time. In the event of a revocation of your consent, the responsible bodies will immediately check to what extent the stored data is still necessary. Data that is no longer required will be deleted immediately and/or biomaterials destroyed, unless there are legal and/or official documentation and reporting obligations to the contrary. However, the data processing carried out until the revocation remains lawful.

You also have the following rights:

Right to information (including free provision of a copy) about your personal data that is collected, processed or, if necessary, transmitted to third parties as part of the study.

Right to rectification of inaccurate personal data, to restriction of processing and to object to the use of the data.

Right to erasure of personal data concerning you, e.g., if this data is no longer needed for the purpose for which it was collected.

Right to restriction of processing: Under certain conditions, you have the right to request a restriction of processing, i.e., the data may only be stored, but not processed. You must apply for this.

Right to data transfer of the data collected about you to a specific location.

Possible restrictions of your rights

The above-mentioned rights may be restricted after examination of the individual case (in particular pursuant to Art. 17 para. 3 lit. d and Art. 89 GDPR). This applies in particular if the application of one of these rights is precluded by contractual, statutory and/or official documentation and reporting obligations or if the execution of the study would thereby be made impossible or seriously impaired.

Exercising your rights

If you wish to claim one or more of the aforementioned rights, please contact the study team of your study center. If you have any concerns about data processing and compliance with data protection requirements, you can also contact the following data protection officers:

zibp – Zentrum für Infektiologie Berlin Prenzlauer Berg GmbH
Driesener-Str. 23
10439 Berlin
datenschutz@zibp.de

You also have the right to raise a complaint with a data protection supervisory authority. If you have any concerns about the handling of your personal data, you can contact the following bodies:

Data protection supervisory authority of the federal state in which your study center is located:
Berlin Commissioner for Data Protection and Freedom of Information
Friedrichstraße 219, 10969 Berlin
Phone: 030 138890mailbox@datenschutz-berlin.de

A list of all data protection supervisory authorities responsible in Germany and the European Union can be found here: https://www.bfdi.bund.de/DE/Service/Anschriften/Laender/Laender-node.html

g) Duration of storage of the data:
The collected data will be stored by the study management and your study center for a period of 10 years after completion or discontinuation of the study.

h) Publication
Scientific publications of results take place in a form that does not allow any direct conclusions to be drawn about your person.

WHOM DO I CONTACT IF I HAVE ANY QUESTIONS?

If you have any questions about this study or if there is a problem, you can contact your study team using the contact details below.

Name: **Stephan Grunwald**

Phone: **030 233 212 870**

E-Mail: **studienzentrum@zibp.de**

Safety and **E**ffectiveness of **MVA**-BN Vaccination against MPXV Infection in at-risk individuals in Germany (**SEMVAc**)

Declaration of Consent

Principal Investigator:

Prof. Dr. med. Leif Erik Sander
PD Dr. med. Florian Kurth
Charité – Universitätsmedizin Berlin
Dept. of Infectious Diseases and Respiratory Medicine
Augustenburger Platz 1
D-13353 Berlin

Study Center:

Dr. med. Axel Baumgarten
zibp – Zentrum für Infektiologie Berlin Prenzlauer Berg GmbH
Driesener-Str. 20/23
10439 Berlin

Last Name:

First Name:

Street:

Postal code and place of residence:

Date of birth:

Telephone No.:

E-mail address:

Participant No.:

Through a personal consultation with

_____

Name of the **study physician**

I have been informed in detail and comprehensibly about the nature, significance, risks and scope of the study. I also read and understood the text of the study information. I had the opportunity to talk about how the study is conducted. All my questions were answered satisfactory.

Possibility to document additional questions or other aspects of the personal consultation:

_____

I had enough time to decide and agree to participate in the study.

I am aware that I can withdraw my consent to participate in the study at any time without giving reasons (orally or in writing) and without incurring any disadvantages. The legality of the data processing until the revocation is not affected by this.

Consent under data protection law:

I am aware that **personal data**, in particular medical findings about me, are to be collected, stored and evaluated in this study. The use of my personal data requires the following voluntary declaration of consent before participating in the study; without the following consent, I cannot participate in the study.

1.I agree that in the context of this study, personal data, in particular information about my health, may be collected about me and recorded in paper form and on electronic data carriers in accordance with the study information. A member of the study team who is obliged to maintain confidentiality can view and scientifically evaluate the data in pseudonymized form in compliance with legal regulations. Provisions may be passed on accordingly. I am aware of the aforementioned legal restrictions on my rights.

2. I agree that my e-mail address will be passed on to the team of the study director for contact in the context of this study (sending questionnaire links).

3. I agree that the data will be kept for 10 years after completion or termination of the study.

4. I agree that up to 10ml of blood is used for serological analyses in the context of routine blood samples.

□ yes, I agree □ no, I don't consent

5. I agree that, if applicable, my **biomaterials** will be retained, used, and disclosed in accordance with the information provided in the study information. I transfer ownership of the biomaterials to the study center.

6. My biomaterials can also be used for further vaccine research:

□ yes, I agree □ no, I don't consent

7. My biomaterials can also be used for other research purposes:

□ yes, I agree □ no, I don't consent

I voluntarily agree to participate
at the above study (SEMVAc).

At the same time, I consent to the processing of my personal data and, if applicable, biomaterials as described and specified by me.

I have received a copy of the study information and consent. One copy remains in the study center.

_____

Name of the **study participant** in block letters

_____

Place/Date — Signature of the **study participant**
(to be signed by the study participant)

I conducted the consultation and obtained the consent of the study participant.

_____

Name of the **study physician** in block letters

_____

Place/Date — Signature of the **study physician**
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Last Name:

First Name:

Street:

Postal code and place of residence:

Date of birth:

Telephone No.:

E-mail address:

Participant No.:

Through a personal consultation with

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Name of the **study participant** in block letters

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Place/Date Signature of the **study participant**
(to be signed by the study participant)

I conducted the consultation and obtained the consent of the study participant.

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Name of the **study physician** in block letters

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