Information for sponsors, applicants and ethics committees concerning “Brexit”

On 29 March 2017 United Kingdom initiated the exit process by written declaration according to Article 50 of the Treaty on the European Union. The withdrawal shall take effect on 29 March 2019. According to the current state of the exit negotiations it is expected that there might be a so called “hard Brexit”. In that case after 29 March 2019 the United Kingdom will neither be part of the European Union (EU) nor a State Party to the Agreement on the European Economic Area (EEA) nor apply other transitional arrangements for the variously affected areas. This would also significantly affect clinical trials of medical devices and medicines and other studies with humans.

A clinical trial of a medicinal product or medical device may only be carried out in Germany (and Europe) if and as long as there is a sponsor or a legal representative of the sponsor whose registered place of business is located in a Member State of the EU or in another State Party to the Agreement on the EEA (see § 40 (1) sent. 3 no. 1 AMG, § 20 (1) sent. 3 no. 1a MPG).

In the case of a "hard Brexit", clinical trials in which the sponsor or legal representative is based in the United Kingdom and where no sponsor or legal representative based in the EU / EEA has been designated until then, must not be continued after the effective date of Brexit. In order to avoid clinical trials and in particular its participants being compromised, it is therefore recommended to nominate a sponsor or legal representative of the sponsor based in the EU or the EEA, timely. Please also take note to the following aspects:

The change of the sponsor or legal representative is a substantial amendment according to § 10 (1) GCP-V and § 22c (3) MPG. This modification may therefore only be implemented after authorization and favorable opinion.

Even though the federal agencies and ethics committees will endeavour for a fast processing, the legal periods of 20 or 30 days for trials with medicinal products and medical devices should be considered. Since a large number of substantial amendments is expected, the modifications relating to the change of sponsor or legal representative should not be combined with other modifications not directly related to the change of the sponsor or the change of the legal representative. Additional claims concerning the other modifications may significantly delay the processing of the modification due to the change of sponsor or legal representative.

Please note that this change may also affect the validity of the existing insurance for clinical trials and that also the insurance carrier must be authorized to conduct business within the EU or the EEA. The change of sponsor or legal representative may also require the policyholder to be corrected in the insurance policy.

The change of the sponsor or legal representative or the insurance carrier also requires a corresponding editorial adjustment of the trial protocol and of the informed consent form (as well as other documents and files, if applicable). These documents should be included in the application to § 10 (1) GCP-V or § 23c (2) No. 2 MPG.

With regard to the informed consent form, it must also be checked whether the information pursuant to Art. 13 or 14 GDPR is up-to-date (person responsible for data processing, data protection officer of the sponsor and / or legal representative, responsible data protection supervisory authority).
In this context, note that a transfer of personal data and / or biomaterial to the United Kingdom in the case of a "hard Brexit" is classified as a transfer to a third country. Then, according to Art. 13 (1) lit. f) GDPR required information needs to be given. The absence of an adequacy decision should be

noted. If the transmission takes place on the basis of suitable or appropriate guarantees (see Articles 46 and 47 GDPR, e.g. "EU standard contractual clauses" or "Binding Corporate Rules"), it must be communicated how to obtain a copy of them or where they are available. In the case of a transfer pursuant according to Art. 49 (1) lit. a GDPR, detailed information about the associated risks is needed as well as an **explicit** consent.

Even though manufacturing and import permits are not part of the assessment of the Ethics Committee, as a precautionary measure, it should be recalled that a “hard Brexit” might have a significant impact in that area, especially in case the import of the IMP into the EU takes place via the United Kingdom or if the medicinal products are manufactured in the United Kingdom. Therefore, appropriate precautions should be taken to ensure uninterrupted availability of the investigational medicinal product in the interest of the trial subjects.

Notification of a substantial Amendment

The submission of an application for a substantial amendment must be done via the DIMDI system in the case of medical device testing. Please update the corresponding information in the notification form (section: sponsor / legal representative). Explain the changes by entering the new sponsor / legal representative and, if applicable, further consequential changes in the notification form and cover letter. If there are changes in the insurance certificate, it must be submitted together with the conditions of insurance.
In case of a clinical trial of a medicinal product, the application for a substantial amendment must be submitted to the competent Ethics Committee in a hard copy together with an electronic data medium (CD). The modifications have to be explained, the new sponsor / legal representative and any further consequential changes in the accompanying letter have to be mentioned. The cover letter must be signed by the sponsor or the legal representative based in the EU / EEA. Otherwise, it may be necessary for the authorized representative to prove his authorization in a suitable form (see § 14 (1) VwVfG). If the information in the insurance policy changes, this must be submitted together with the conditions of insurance.

Studies that do not fall under the provisions of §§ 40 ff AMG or §§ 20 ff MPG

Even in studies that do not fall under the provisions of §§ 40 ff AMG or §§20 ff MPG, there may be consequences in the case of a "hard Brexit". In particular, the transmission of personal data and samples as well as any existing insurance should be checked accordingly.

Checklist

Question		**Remarks**	**Assessment by the ethics committee (EC)**
Sponsor/legal representative based in the EU/EEA?		accompanying letter (as well as notification form, if applicable)	+
Is the insurance valid?		Hand in the renewed insurance certificate and conditions, if applicable	+ (the validity of the insurance will be checked in any case)
	Is the insurance company based in the EU/EEA?		+
	Policyholder?		+
Informed consent form(s)		Should be handed in with application according to § 10 (1) GCP-V and § 22c (2) no. 2 MPG	It is at the discretion of the EC to review editorially corrected documents in a cursory manner and to provide notes if necessary
	Sponsor/legal representative		
	person responsible for data processing		
	data protection officer of the sponsor / legal representative		
	responsible data protection supervisory authority of the sponsor / legal representative		
	Information about the transfer to a third country		
Protocol	Current sponsor	Should be handed in with application according to § 10 (1) GCP-V and § 22c (2) no. 2 MPG	It is at the discretion of the EC to review editorially corrected documents in a cursory manner and to provide notes if necessary
Is the uninterrupted availability of the investigational medicinal product ensured?			Although, not in the primary area of responsibility of the EC, a lack of medicinal products supply may still lead to withdrawal