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Questions and answers – Clinical Trials Information System (CTIS) and Clinical Trials Regulation (CTR)

Prepared by the Query Management Working Group

Important notice: The views expressed in this questions and answers (Q&A) document are not legally binding. The European Court of Justice is the only authority that can give an authoritative interpretation of Community law. This document aims at informing on the technical aspects of the Clinical Trials Regulation (EU) No 536/2014 with a view to facilitating its implementation.

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1. Introduction

This document provides answers to questions regarding CTIS and the CTR that were raised by representatives of sponsor associations, including the Association of Clinical Research Organisations (ACRO), the European Federation of Pharmaceutical Industries and Associations (EFPIA), the European Confederation of Pharmaceutical Entrepreneurs (EUCOPE) and the European Clinical Research Organisation Federation (EUCROF).

All updates to this Q&A document have been discussed within the Query Management Working Group and reflect the view of the group. This group is chaired by the European Medicines Agency (EMA) and composed of representatives of the Clinical Trials Coordination Group (CTCG), the Expert Group on Clinical Trials (CTEG) and the European Commission (EC).

2. List of Acronyms

ACRO - Association of Clinical Research Organisations

AR – Assessment Report

ASR – Annual Safety Report

AxMP – Auxiliary Medicinal Product

CCI - Commercially Confidential Information

CRO – Clinical Research Organisation

CSR – Clinical Study Report

CT – Clinical Trial

CTA – Clinical Trial Application

CTCG – Clinical Trials Coordination Group

CTD – Clinical Trials Directive No. 2001/20/EC

CTEG – Expert Group on Clinical Trials

CTFG – Clinical Trials Facilitation Group

CTIS – Clinical Trials Information System

CTR – Clinical Trials Regulation No. 536/2014

DSMB - Data and Safety Monitoring Board

EC – European Commission

EthC – Ethics Committee

EFPIA – European Federation of Pharmaceutical Industries and Associations

EMA – European Medicines Agency

EU – European Union

EUCOPE – European Confederation of Pharmaceutical Entrepreneurs

EUCROF – European Clinical Research Organisation Federation

EV – EudraVigilance

EVPM – EudraVigilance Post-Authorisation Module

EVCTM – EudraVigilance Clinical Trial Module

GCP - ICH E6 (R2) Good Clinical Practice

GDPR – General Data Protection Regulation No. 2016/679

GMO - Genetically Modified Organism

IAM – EMA Account Management

ICH – International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

IMP – Investigational Medicinal Product

IMPD – Investigational Medicinal Product Dossier

MA – Marketing Authorization

MAA – Marketing

MS – Member State

MSC – Member State Concerned

NCA – National Competent Authority

NSM – Non-substantial modification

OMS – Organisation Management Service

PD – Personal Data

PPD – Protection of Personal Data

PMS – Product Management Service

RFI – Request for supplementary information

RMS – Reporting Member State

SAE – Serious Adverse Event

SAR – Serious Adverse Reaction

SM – Substantial Modification

SPOR –Substance, product, organisation and referential data management services

SUSAR – Suspected Unexpected Serious Adverse Reaction

xEVMPD – Extended EudraVigilance Medicinal Product Dictionary

xEVPRM – Extended EudraVigilance Product Report Message

3. Useful references

This table lists the referenced documents in this Q&A with their online location.

Reference	Location
Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014	https://www.ema.europa.eu/en/documents/other/appendix-disclosure-rules-functional-specifications-eu-portal-eu-database-be-audited_en.pdf
Clinical Trials Information System (CTIS): online modular training programme (Module 1 to Module 24)	https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-information-system-ctis-online-modular-training-programme#sponsor-workspace-section
Clinical trials - Regulation EU No 536/2014	https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32014R0536
Clinical trials in the European Union (CTIS)	https://euclinicaltrials.eu/
Communication from the Commission — Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3')	Communication from the Commission — Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use (CT-3) (europa.eu)
CTIS User support service	https://euclinicaltrials.eu/support-info/#support-user-support
CTFG Best Practice Guide for sponsors of multinational clinical trials with different protocol versions approved in different Member States under Directive 2001/20/EC that will transition to Regulation (EU) No. 536/2014	https://www.hma.eu/fileadmin/dateien/Human_Medicines/01-About_HMA/Working_Groups/CTFG/2018_05_CTFG_Best_Practice_Guide_for_sponsors_of_transition_multinational_clinical_trials.pdf
Document codes and titles in CTIS	https://www.hma.eu/fileadmin/dateien/HMA_joint/00-_About_HMA/03-Working_Groups/CTCG/2022_09_CTCG_Instruction_naming_documents_CTIS_EU_v1.4.pdf
[DRAFT] Guidance document on how to approach the protection of personal data and commercially confidential information in documents uploaded and published in the Clinical Trial Information System (CTIS)	https://www.ema.europa.eu/en/documents/other/draft-guidance-document-how-approach-protection-personal-data-commercially-confidential-information_en.pdf
EMA Account Management | Frequently Asked Questions (FAQ)	https://register.ema.europa.eu/identityiq/help/faq.html

Reference	Location
EudraLex - Volume 10 - Clinical trials guidelines, including the Questions and Answers document, that is regularly updated	https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-10_en#set-of-documents-applicable-to-clinical-trials-that-will-be-authorised-under-regulation-eu-no-5362014-once-it-becomes-applicable
EMA Account Management Training Session presentation slides	https://www.ema.europa.eu/en/documents/presentation/presentation-ema-account-management-training-session_en.pdf
European Medicines Agency - Clinical trials in human medicines	https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials-human-medicines#clinical-trials-regulation-section
European Medicines Agency - Substance and product data management services	https://www.ema.europa.eu/en/human-regulatory/research-development/data-medicines-iso-idmp-standards/spor-master-data/substance-product-data-management-services
Guideline for the notification of serious breaches of Regulation (EU) No 536/2014 or the clinical trial protocol	https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-notification-serious-breaches-regulation-eu-no-536/2014-clinical-trial-protocol_en.pdf
ISO IDMP standards	https://www.ema.europa.eu/en/human-regulatory/overview/data-medicines-iso-idmp-standards-overview
Joint Controllership arrangement (JCA)	https://www.ema.europa.eu/en/documents/other/joint-controllership-arrangement-regard-clinical-trials-information-system-ctis_en.pdf
Q&A on the protection of commercially confidential information and personal data while using CTIS	https://www.ema.europa.eu/en/documents/other/questions-answers-protection-commercially-confidential-information-personal-data-while-using-ctis_en.pdf
Q&A on the JCA	https://www.ema.europa.eu/en/documents/other/questions-answers-joint-controllership-arrangement-data-protection-matters-related-use-clinical_en.pdf
Regulation (EU) 536/2014 on clinical trials – list of national contact points	https://health.ec.europa.eu/medicinal-products/clinical-trials/clinical-trials-regulation-eu-no-5362014_en (Under section "Contact points")
Sponsors Handbook	https://www.ema.europa.eu/en/documents/other/clinical-trial-information-system-ctis-sponsor-handbook_en.pdf
SPOR data management services	https://spor.ema.europa.eu/sporwi/

Reference	Location
Timelines document	https://www.ema.europa.eu/en/documents/other/clinical-trial-information-system-ctis-evaluation-timelines_en.pdf

Questions and answers

The questions related to CTIS and the CTR, received from the different stakeholders mentioned above, were collected and categorised by themes. Each category is presented in the table below along with the questions and answers provided by the Query Management Working Group.

Q. No.	Category	Question	Response
1.	Assessment	What's the process of handling RFIs in CTIS? Are there any rules on who can receive notifications? Are there any requirements in terms of the format of RFIs and answers? Is there a functionality to download the RFI?	In order to prepare an RFI, considerations are consolidated for Part I and Part II by the Reporting Member State (RMS) in the validation phase, by the RMS during the Part I assessment, and by the Member States Concerned (MSC) during the Part II assessment. According to best practice, assessors should only raise one RFI if needed. However, if the response does not sufficiently address the considerations, a follow-up RFI might be raised. In procedures where no validation is foreseen, there could be an RFI with a short deadline followed by a regular RFI. To reply to an RFI, it is necessary to complete all the "response" free text boxes and optionally, supporting documentation can be provided with each of the considerations raised in the RFI. The sponsor can modify the dossier by uploading a new document, updating an existing document, or updating the structure data (functionality across the system). In order to download an RFI, the 'evaluation' section of the download functionality can be accessed. The format of the RFI content is rendered in a PDF that can be downloaded. See Training module 9 "How to view and download clinical trial (CT) information". Relevant training materials explaining the process and the rules about RFIs in CTIS are available in Training module 11 and in the Sponsor Handbook.

Q. No.	Category	Question	Response
2.	Assessment	How are the original and updated documents stored in the system (naming, numbering)? Is it possible to see the original documents after uploading the updated version in CTIS?	When a document is updated using the update functionality, the metadata such as the document name (title), type and language remain unchanged, and the system versioning is incremented for the new document. However, the sponsor can provide the document date and sponsor version of this updated document. All users can see the metadata pertaining to each document version. See relevant information in Training module 11 and the Sponsor Handbook. In the secure website the documents are presented according to their metadata (including document type, title and (system) version) for each trial, in the "Full trial information" tab under the "all documents" section.
3.	Assessment	Can an RFI response due date fall on a weekend or public holiday?	The sponsor due date for an RFI cannot fall on a weekend or during the winter clock stop but may fall on a public holiday. For further information, refer to the Timelines document.

Q. No.	Category	Question	Response
4.	Assessment	Should the MS issue the list of the EthC members involved with the assessment for compliance with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) E6 (R2) Good Clinical Practice (GCP)?	As stated in GCP, sponsors and investigators need to comply with the applicable regulatory requirements. The CTR takes precedence over conflicting rules in guidelines, and that is applicable to GCP as well as other guidelines. Documents or data that are not described by the CTR shall not be requested or submitted based on recommendations in different guidelines. This is also applicable to the composition of the EthC. According to Article 9 of the CTR, it is up to the MS to assure the adequate composition of the EthC, and it is not required for the MS to provide the list of the EthC members involved with the assessment to the sponsor. The single decision, per MS, on each CTA and subsequent changes to that application at the MSs level represents the outcome of a scientific and ethical review, involving an EthC, in compliance with the CTR and in accordance with the national law of the MSC.
5.	Assessment	Is there a possibility to communicate with the RMS via CTIS during the evaluation of a CTA and especially at the time of an RFI response?	The only possibility to communicate with the RMS via CTIS is by responding to the RFI. Any other communication needs to occur outside the system, and national contact points can be approached if clarification is needed. See Q1.4 point 8 of the EudraLex – Volume 10 Q&A.
6.	Assessment	Part II Application: Can National Competent Authorities (NCAs) ask for additional documents that are not listed in Annex I of the Regulation, like a Power of attorney for a third organisation (e.g. Clinical Research Organisation (CRO)) in that country?	The CTR provides the list of document and information requirements, for both the EthC and the competent authority in the concerned Member State for a CTA. Further clarifications have been provided in the Q&A published by the EC in particular for documents in Part II. The submission needs to be in compliance with the CTR (in particular with Annex I and II), adapted as necessary in line with the national legislation when allowed by the CTR (for example with regards to damage compensation, financial agreements, proof of payment). Documents like the Power of attorney and CT progress reports are not defined by CTR, therefore they are not required.

Q. No.	Category	Question	Response
7.	Assessment	What is the process for responding to MS queries/questions on serious breaches notifications? Is it mandatory to have dedicated/nominated person for notifications including serious breaches?	In CTIS, MSC can assess notifications, including serious breaches, using the ad-hoc assessment functionality, and involve all MSCs and others who are affected. They can raise an RFI to the sponsor if necessary. In case an RFI is raised, the sponsor will receive a notification in the Notice & Alert tab, and the RFI will also be displayed in the RFI tab. The sponsor role required to prepare and/or submit a response to this type of RFI is the Notification preparer or submitter, on top of the CT Admin role.
8.	Assessment	Can a serious breach submission be done for several trials?	If the same serious breach affects several trials, the sponsor needs to submit individual notifications for each of them. Refer to 'Appendix III b – Information to be submitted with a notification of a serious breach' in the 'Guideline for the notification of serious breaches of Regulation (EU) No 536/2014 or the clinical trial protocol' document. In question A5 the sponsor can clarify if one or more trials are affected by the breach, but individual notifications for each clinical trial still need to be submitted in CTIS.
9.	Assessment	How can the sponsor monitor messages and information that have been submitted to the sponsor if there is no emailing functionality?	The system informs the users about events occurring during the trial lifecycle. The users are expected to interact with the system and centrally review the information or request provided by the MS. Therefore, the sponsor needs to monitor the notices and alerts tab and the RFI tab.
10.	Clinical Trial Application under the CTR	Should the documents be uploaded with signature? Do the CTIS electronic submissions with sponsor user dialogue windows (e.g. "submit application", "submit RFI response") fulfil the requirement of Annex I, A.3 and II, A.2?	CTR requires the application to be signed, and this obligation is fulfilled when the user logs in to the system, considering the approach to user management in CTIS. See the EudraLex – Volume 10 Q&A, that specifies what document/data shall be submitted with an application, including instructions on the signature.

Q. No.	Category	Question	Response
11.	Clinical Trial Application under the CTR	CTIS Part I Section: Protocol Synopsis / Expectations on document format Does the protocol synopsis need to be provided in lay language as a separate attachment to the protocol?	According to the EudraLex – Volume 10 Q&A, the synopsis can be part of the protocol or submitted as a separate document, especially to address different language versions. The content of the synopsis is proposed in the Q&A and it is stated that sponsors should consider making the synopsis understandable to a layperson.
12.	Clinical Trial Application under the CTR	CTIS Part I Section: Data and Safety Monitoring Board (DSMB) Charter Are there any legal expectations on the format of the Data and Safety Monitoring Board (DSMB) charter? Will sponsors need to submit the DSMB charter only, or a DSMB charter with all Committee members listed? Will it need to be signed and if yes, what signature format (wet-ink or electronic) would be expected?	There are no requirements on the format of the DSMB charter. The CTR requires the submission of the DSMB charter when applicable. It is not required for the DSMB charter to be signed.
13.	Clinical Trial Application under the CTR	CTIS Part I Section: Document translations Regarding the EudraLex - Volume 10 Q&A, Annex II on Language requirements for Part I documents, when an MSC requests translations for data and documents, does it refer only to documents "for publication"? Should the extract of document(s) as referred to in Annex I also be translated?	The legislation does not differ between "for publication" and "not for publication" documents, and the translations should be provided as outlined in the EudraLex – Volume 10 Q&A, Annex II. The provision for translations also applies to the "extract" version of the documents.
14.	Clinical Trial Application under the CTR	Do the documents required under the CTD need to be submitted to CTIS, if not mentioned in Annex I and II of the CTR?	Only the documents required by the CTR and the Q&A should be uploaded in CTIS. For further information see Q1.4 and Q1.5 in the EudraLex – Volume 10 Q&A.

Q. No.	Category	Question	Response
15.	Clinical Trial Application under the CTR	CTIS Part II Section: Financial and other arrangements Annex I, P. 71 states 'Description of any other agreement between the sponsor and the site shall be submitted'. Would a description of any other agreement be sufficient?	The requirement is MS specific and needs to be consulted with each MSC. To describe arrangements for the compensation for trial participants, sponsors are encouraged to use the dedicated harmonised template as mentioned in the document' Set of documents applicable to clinical trials authorised under Regulation EU No 536/2014'.
16.	Clinical Trial Application under the CTR	CTIS Part II Section: Recruitment arrangements (Annex I, K / Article 7.1 (c)) In relation to the template document 'Recruitment and Informed consent procedure template' (version 3.0 Nov 2019), the same template document supports two different CTIS upload slots (recruitment arrangements, and informed consent). Can further information be provided? As the current template may confuse sponsors and lead to inconsistent implementation.	The recruitment and informed consent procedure template document supports two different CTIS upload slots. It can be used to prepare the two supportive documents, that should be uploaded in each slot. The text of the informed consent also needs to be uploaded, as well as the advertising material (under Annex I, K).
17.	Clinical Trial Application under the CTR	CTIS Part II Section: Suitability of the investigator (Annex I, M & N / Article 7.1 (e) & Article 49) EudraLex Volume 10, Chapter I Harmonization Guideline states that documentation related to investigators who are not the principal investigator or the responsible leader of a team of investigators (i.e. sub-investigators), may need to be submitted in Part II for an MSC, if the national requirements specify. When will sponsors know, if MSs plan to request CVs, GCP evidence, and declaration of interests also for other investigators (i.e., sub-investigators)?	In general, these aspects are covered under suitability of the investigator and site suitability in Annex I, M (64&65) & N (67) and thus additional documentary requirements seem to be redundant. Only the changes in Principal Investigator need to be submitted as SM applications.

Q. No.	Category	Question	Response
		Is it appropriate to assume, that changes to sub-investigators will not constitute Part II SM, which Article 15 only defines for principal investigators?	
18.	Clinical Trial Application under the CTR	What will be the language of the RFI relating to Part II, considering that during the validation all questions will be sent via the RMS in one RFI?	It is likely that the language of the document referred to in the question would drive the language of the consideration. It is within the remit of each MSC to decide the language, including validation considerations (Art 26 of CTR).
19.	Clinical Trial Application under the CTR	Labels languages in EudraLex – Volume 10 Q&A guidance Some MSs (e.g. Denmark and Sweden) appear not to accept English for products administered at site, is this correct?	Labelling is subject to national decisions and some MSs are accepting labelling in English, if justification is provided. Refer to EudraLex – Volume 10 Q&A, Annex II.
20.	Clinical Trial Application under the CTR	Where can the sponsor find clarification on the definition of Low Interventional CT?	See Q1.6 of the EudraLex - Volume 10 Q&A and the Guidance on risk-appropriate approach in CTs.
21.	Clinical Trial Application under the CTR	Is it acceptable to only submit the financial disclosure form rather than the declaration of interest?	The CTR requires a declaration of financial interest for the disclosure of possible or actual conflicts of interest. Refer to the proposed Declaration of Interest template available on the EC website. The financial disclosure can be submitted as a supporting document, along with the declaration of interest form.
22.	Clinical Trial Application under the CTR	Regarding the financial arrangements between the sponsor and the sites, would a proposal (or proposal and agreement statement) be acceptable for an application?	Submission of a proposal is satisfactory if the details provided are sufficient for an assessment.

Q. No.	Category	Question	Response
23.	Clinical Trial Application under the CTR	According to Annex I of the CTR (L. 61.), all information given to the subjects (or, where applicable, to their legally designated representatives) before their decision to participate or abstain from participation, shall be submitted together with the form for written informed consent, or other alternative means according to Article 29 (1) for recording informed consent. The CTR does not mention other patient-faced materials, such as diaries, patient reported outcome questionnaires, etc. Should diaries, ePROs and similar patient-faced materials need to be included in the Part II dossier according to the CTR?	Refer to Q.1.24 EudraLex – Volume 10 and its Q&A document on patient facing documents. Patient facing documents are documents, other than recruitment material or subject information sheets, presented to clinical trial participants during the conduct of the clinical trial. These can be questionnaires, patient diary, patient card or patient reported outcomes (PRO/ePRO).
24.	Clinical Trial Application under the CTR	Annex I of the CTR (D. 17 (g)) states that the protocol shall include "a statement of whether the investigational medicinal products and auxiliary medicinal products used in the clinical trial are authorised; if authorised, whether they are to be used in the clinical trial in accordance with the terms of their marketing authorisations, and, if not authorised, a justification for the use of non-authorised auxiliary medicinal products in the clinical trial". What's the process if an AxMP used in the clinical trial is authorised in some EU countries but to be used in other EU countries? Or if the AxPM is not used in accordance with the terms of its marketing authorisations?	Regarding supply, it should be possible for the sponsor to provide the AxMPs centrally in countries where the product is not authorised, as local supply through pharmacies is normally not possible for unauthorised AxMPs. Where the product is authorised, it can be supplied centrally or locally. Preferably, this should be clearly specified in the protocol (or cover letter), i.e. in which countries local resp. central supply is used. The documentation requirements (labelling, GMP-verification) will differ depending on local or central supply. Recommendation on AxMPs in CTs is available in EudraLex – Volume 10. Similar rules apply as for an IMP also with regards to authorisation status, see Table 1 (content of the simplified IMP Dossier) of Annex I of the CTR.

Q. No.	Category	Question	Response
25.	Clinical Trial Application under the CTR	Annex I of the CTR (D.17 (g)) states that the protocol shall include "a statement of whether the investigational medicinal products and auxiliary medicinal products used in the clinical trial are authorised; if authorised, whether they are to be used in the clinical trial in accordance with the terms of their marketing authorisations, and, if not authorised, a justification for the use of non-authorised auxiliary medicinal products in the clinical trial". a) Does the sponsor have to centrally supply the unauthorised AxMP to all MS or can it be sourced locally and reimbursed by the sponsor? b) Should the sponsor provide the authorised AxMP for free? c) What are the guidelines governing supply and reimbursement in case a product is an authorised AxMP in some MSs and unauthorised AxMP in another MS?	a) The sponsor should supply unauthorised AxMPs centrally, as local supply through pharmacies is normally not possible for unauthorised AxMPs. b) Yes, see Article 92 of the CTR for details: "Investigational medicinal products, other products and procedures, free of charge for the subject: Without prejudice to the Member States' competence for the definition of their health policy and for the organisation and delivery of health services and medical care, the costs for investigational medicinal products, auxiliary medicinal products, medical devices used for their administration and procedures specifically required by the protocol shall not be borne by the subject, unless the law of the Member State concerned provides otherwise." c) Regarding supply, it should be possible for the sponsor to provide the AxMPs centrally in countries where the product is not authorised, as local supply through pharmacies is normally not possible for unauthorised AxMPs. Where the product is authorised, it can be supplied centrally or locally. Preferably, this should be clearly specified in the protocol (or cover letter), i.e. in which countries local resp. central supply is used. The documentation requirements (labelling, GMP-verification) will differ depending on local or central supply. See recommendation on AxMPs in CTs in the EudraLex – Volume 10 and its Q&A document.
26.	Clinical Trial Application under the CTR	How should non-substantial quality modifications relevant to the supervision of the trial (Art 81.9 change) be uploaded into CTIS? What documentation is required?	Non-substantial changes to the investigational medicinal product dossiers (IMPD) should be implemented during the next SM, whenever the scope of the non-substantial changes matches with the scope of the application under evaluation. For further details see Q3.4. in the EudraLex – Volume 10 Q&A: 'What are the sponsor's responsibilities regarding changes to a clinical trial, which are non-substantial modifications (NSM)?'

Q. No.	Category	Question	Response
27.	Clinical Trial Application under the CTR	Based on differing local requirements for the treatment with radiopharmaceuticals, studies with radiopharmaceuticals often need to accommodate these by local protocol amendments. How is this handled under the CTR?	Exceptionally, if there is a need for national provisions in relation to treatment with radiopharmaceuticals*, the sponsor needs to highlight the national provisions for the MSC in the relevant section of the [consolidated] protocol, or in its Annex. During the Part I assessment the RMS will rely on the feedback of the MSC if these national provisions are acceptable. *e.g. when required by national legislation on nuclear safety protection
28.	CTIS Implementation	Is there a plan to include in CTIS a technical tool for automatic redaction of documents that are required to be uploaded for publication?	Inclusion of a redaction tool in CTIS is not foreseen.
29.	CTIS Implementation	What are the character limits for the different free text structured data fields and the document titles in CTIS?	Data fields and document specifications can be found in the EMA training materials, in the training and support section, "reference materials for clinical trial sponsors" sub section. As a general rule, the limitation for free text fields is 4000 characters. In some cases this limitation is less, as specified in the Sponsor Handbook.
30.	CTIS Implementation	Are there any plans for linking submissions in CTIS with 3rd body radiology, for Genetically Modified Organisms (GMO), medical device submissions performed at a national level, considering that the final trial decision should account for all aspects of the protocol and product? Specifically for GMO advanced therapy medicinal product submissions, what will be the process for those countries where a consolidated CTA and GMO submission is currently made under the Directive? Would a separate submission be needed outside of CTIS to the same agency? Are there any plans for linking CTIS and the new	At present no interchange or linking between CTR/CTIS and other legislation/systems is foreseen. Risks to the environment caused by an IMP is not within the remit of the CTR (ARTICLE 6.(1) (b) ii - only risks to the subject). In practice, a sponsor needs to do one submission through CTIS, and separate ones to each MS for the GMO aspects as applicable.

Q. No.	Category	Question	Response
		Medical Device Regulation (MDR) and the In Vitro Diagnostic Regulation (IVDR) portal?	
31.	GDPR	In Annex I of the CTR (R) of Part II documents "Proof that data will be processed in compliance with Union law on data protection", it is specified that "A statement by the sponsor or his or her representative that data will be collected and processed in accordance with Directive 95/46/EEC shall be provided." How does it work in practice? Is there a template document that needs to be signed and uploaded in CITIS?	A placeholder for a statement of compliance with General Data Protection Regulation No. 2016/679 (GDPR) is currently present in the system, and it is located in the CTA under the 'Form' section. The sponsor can upload in that section the statement of compliance with GDPR principles. A template is published in EudraLex – Volume 10 - Clinical trials guidelines.
32.	GDPR	To avoid any GDPR/confidentiality issue, is it acceptable to use generic email addresses in the sponsor contacts section?	In CTA/Part I, Scientific and public contact points are subject to publication rules, and should be provided with functional contact details (functional department and functional e-mail addresses). See section 4.2 of the Appendix on disclosure rules (EMA/42176/2014). In CTA/Part I, the "contact point for union" is not subject to publication rules and should be provided with contact details of a natural person, to enable the member states and the EMA to directly contact them if necessary.
33.	Master Data Sources (SPOR / xEVMPD)	The EMA training material is referencing the Extended EudraVigilance Medicinal product Dictionary (xEVMPD) and the Organisation Management Service (OMS). Also, in some presentations there is reference to the substance, product, organisation and referential data management services (SPOR). What is the link between xEVMPD and SPOR?	SPOR is a platform that integrates various databases, including OMS. RMS provides referential lists and terms (such as routes of administration, dosage forms) in multiple languages. EMA is implementing the ISO IDMP standards in pharmaceutical regulatory processes based on the four domains of master data: substance, product, organisation and referential (SPOR) master data. Although ISO IDMP covers the entire medicinal product lifecycle, including products in development, investigational products,

Q. No.	Category	Question	Response
			products under evaluation and authorised products, the first iteration of the Product Management Service (PMS) covers only a subset of the authorised medicinal product part of the ISO IDMP standards. The submission and maintenance of data on authorised human medicines, mandatory since July 2012, is currently based on a format called Extended EudraVigilance Product Report Message (xEVPRM) and is used to populate the Extended EudraVigilance Medicinal product Dictionary (xEVMPD). With the implementation of the SPOR programme, xEVPRM will be replaced by the ISO IDMP compatible format, and xEVMPD will be replaced by the PMS. The submission and maintenance of data on human development, investigational products, products under evaluation are not affected, it continues to be based on the xEVPRM, and it is used to populate the xEVMPD.
34.	Master Data Sources (SPOR / xEVMPD)	What is the current expectation in relation to the timing of implementation of SMS and PMS as the source of IMP-related information for the application form within CTIS? Is there any information available on the transition from xEVMPD to SPOR?	Since July 2019, SMS is the source of substance data for IMPs. All substances are registered in SMS and then synchronised with XEVMPD and can be used searched and selected in CTIS for authorised products. Further information on the substance and product data management services is available on the EMA website on the 'Substance and product data management services' page.
35.	Master Data Sources (SPOR / xEVMPD)	Which organisations in CTIS need to have an OMS ID? What are the implications for a CTIS application if the OMS details are not available or not correct?	It is not mandatory, but highly recommended to register the organisation in OMS in advance of submission. Also, registration of sites directly in CTIS is available for the following five areas of the system: Third-party organisations (Part I/Sponsor section), Trial sites (Part II), Details of the site where the serious breach occurred (Serious Breach Notification), Third country inspection site (Third Country inspectorate Notification), Inspected site (MS Inspections).

Q. No.	Category	Question	Response
			Organisations created locally in CTIS behave and function in the same way as the ones sourced from the Organisation Management Service (OMS), and can be searched and selected once they have been registered in CTIS. See also the Sponsor Handbook for further information.
36.	Non-EEA 3rd countries	Since the EU CTR does not repeal the Paediatric Regulation, how should the CTs be managed which are conducted under a PIP, but solely in non-EEA 3rd countries? In EudraCT it's possible to have a 3rd country CTA form submitted to EMA. In CTIS, it's not possible to create an EU CT number and submit a CT dossier to EMA.	Trials conducted in 3rd countries (non-EU, non-EEA) must be submitted in EudraCT until CTIS can accommodate this requirement.
37.	Non-EEA 3rd countries	Can one inspection report be associated to multiple studies, or does it need to be submitted for each study individually?	An inspection report from a 3rd country inspectorate can only be associated with one study individually and be submitted for a specific study.
38.	Safety / ASR	In the CTR Q&A it is clarified that an IMP is a medicinal product that is being tested or used as a reference, including as a placebo in a CT. According to Article 43 of the CTR, an Annual Safety Report (ASR) is required for all IMPs other than placebos. For a reference compound (active or placebo), safety information could also be taken up in the ASR of the test IMP. Would a listing of SAR be sufficient?	A listing of SAR is not regarded as sufficient. As per ICH E2F, the Development Safety Update Report (DSUR) should concentrate primarily on the investigational drug, providing information on comparators (like reference compounds including placebos) only where relevant to the safety of trial subjects. Summary tabulations of all Serious Adverse Event / Serious Adverse reaction (SAE/SAR) for the IMP and comparators should be included in the ASR, e.g. in the cumulative summary table of SAE/SAR. An analysis of observations and their impact on safety profile with focus on changes, including benefit-risk for the CTs in the respective chapters of the ASR (e.g. section 8 findings in CTs, section 11 marketing experience, and especially in sections 18-20) and if applicable risk mitigation is expected.

Q. No.	Category	Question	Response
39.	Safety / ASR	Is it required to submit the ASR directly to the Ethics Committee and can it be done via the EV database?	It is not possible to submit ASR to the EV database directly, ASRs have to be submitted via CTIS. However, if some trials are still running under the CTD, sponsors are still obliged as per CT-3 to submit ASRs to Ethics Committees according to national legislations. See answer to Questions 7.29 and 7.49 in the EudraLex – Volume 10 Q&A, that clarify the scenario for the submission of ASR to the Ethics Committees.
40.	Safety / SUSAR	In reference to the CTR Q&A 7.32, should pregnancy reports, medication errors and misuse in CTs only be submitted to the EudraVigilance CT Module (EVCTM) as expedited reports, if there is an associated SUSAR reported?	As per CTR, medication errors, pregnancies and uses outside what is foreseen in the protocol, including misuse and abuse of the product, shall be subject to the same obligation to report as adverse reactions. However, although information on the occurrence of such events should always be collected by the sponsor, expedited reporting to EVCTM as SUSAR is required only if these events are associated with harm for the subject/adverse outcome of the pregnancy/foetus and this is assessed as «serious» (by either the investigator or the sponsor) (always, in case of adverse pregnancy outcomes). Finally, information on the occurrence of these events with or without adverse events associated need to be reported and analysed in the ASR (see ICH E2F).
41.	Safety / SUSAR	Answer to Q7.30 in the EudraLex – Volume 10 Q&A on sending SUSARs to investigators of a clinical trial states, that the reporting of all SUSARS to all concerned investigators/institutions should be expedited. It also states that the most important thing is to inform investigators of safety profile changes, not of individual SUSAR reports. When is it required to report individual SUSARS to investigators? Does it apply to open or blinded SUSARS and SSRs?	Reporting of safety information to investigators is expected under the CTD/CTR. Overall, it is important that the investigators are informed about changes in safety profile, potential risks, and their mitigation. Therefore, individual SUSAR report is not to be provided as such to investigators. The information should be concise and practical. Therefore, the information on SUSARs should be aggregated in a line listing of SUSARs in periods as warranted by the nature of the research project/clinical development project and the volume of SUSARs generated. This line listing should be accompanied by a concise summary of the evolving safety profile of the IMP and an updated benefit risk.

Q. No.	Category	Question	Response
			Investigators should only receive blinded information, unless unblinded information is judged necessary for safety reasons (see ICH E2A).
42.	Safety / SUSAR	Regarding Q7.26. in the EudraLex – Volume 10 Q&A on SUSAR reporting: Is the treatment allocation that the participant has received in a blinded study required to be stated in the narrative for expedited SUSAR reporting, or only if the reference in 7.26 (n) is for end of study unblinding?	Unblinding is expected when needed to appropriately treat subjects, e.g. to mitigate risks in case of a SUSAR. In case not unblinded by investigator, the narrative will be blind, and require unblinding by sponsor for safety reporting to competent authorities via the EudraVigilance (EV) database. As per CTR: If following unblinding an event turns out to be a SUSAR, the reporting rules for SUSARs set out in Article 42 and in Section 2 of Annex III shall apply.
43.	Safety / SUSAR	Article 46 of the CTR states that "Safety reporting with regard to auxiliary medicinal products shall be made in accordance with Chapter 3 of Title IX of Directive 2001/83/EC". Is there a requirement for submission and approval of AxMP SmPCs if the safety information is updated in the relevant SmPC?	AxMP supporting documents and requirements are similar to IMP requirements. In case there is an updated SmPC for a medicinal product used as AxMP, which has significant impact on the safety or rights of the subjects and/or the reliability and robustness of the data generated in the CT, it is regarded as an SM and required to be submitted as such. Adverse reactions to authorised AxMP during CTs should be reported to EudraVigilance Post-Authorisation Module (EVPM) (as for post-marketing spontaneous reports), according to Chapter 3 of Title IX of Directive 2001/83/EC).
44.	Training & Support	Regarding the list of data fields that need to be completed in CTIS, what are the requirements in terms of the format of the information that need to be uploaded? Which information will be disclosed? Which data fields are mandatory?	This information is available in the CTIS Structured data forms, which can be found in the Sponsor Handbook. Refer to column "Field Type" in each "CTIS Structured data form" excel file. Refer to column "Conformance" in each "CTIS Structured data form" excel file. There is a technical validation in CTIS ensuring completeness of all mandatory structured data fields and documents already upon submission. Refer to column "Publication" in each "CTIS Structured data form" excel file.

Q. No.	Category	Question	Response
			Specifically, the CTIS Structured data form for initial application, additional MSC, SM and NSM contains information whether a field is editable or not in a NSM.
45.	Training & Support	Is there a naming convention for the documents that need to be uploaded in CTIS?	The naming convention document is referenced in the Sponsor Handbook "CTCG's Best Practice Guide for Sponsors of document naming in CTIS". There are some technical restrictions, for example special characters (e.g. /, . ; |) are not allowed. The name of a specific document should not contain the version number of that document, this has to be provided in the document metadata instead. When the user updates a document with a new version, the document will have the same document type, language and title as before.
46.	Training & Support	Regarding the documents that need to be uploaded in CTIS, are there any formatting requirements/restrictions (e.g. PDF version, security settings, wet signatures/eSignatures etc.)?	CTIS Structured data forms provide information on the document format and restrictions required (.PDF, .Doc, 50MB etc.) for each document (refer to column "Document format" in each "CTIS Structured data form" excel file). CTIS has an antivirus verification setting to enable the upload of documents, eSignatures, etc. It must be a valid format file that can be read by an authorised user. In general, documents should exclude signatures. Refer to the EudraLex – Volume 10 Q&A document Q.1.4 to find out on the requirements for documents that should be provided with a signature (e-signature or wet ink signature). CTR requires the application to be signed, this obligation is fulfilled when the user logs in to the system, considering the approach to user management in CTIS. Documents should be searchable and allow copy & paste, i.e., security restrictions should not be included in the document settings.

Q. No.	Category	Question	Response
47.	Training & Support	What information needs to be provided during the uploading of a document, and how are the document properties managed in CTIS?	Sponsor users need to consider that the 'for publication' version of the documents will be published, so it is their responsibility to follow the GDPR for the protection of personal data (PPD) when this is needed. Any personal information provided in the document properties or content is governed by PPD rules applied to any CTIS content. See the Sponsors Handbook for further information.
48.	Training & Support	What are the requirements regarding the submission of the track changed and clean version of a document in relation to the selection 'for publication' or 'not for publication'?	When sponsors submit an SM, of any type, they have to provide a mandatory document with an extract of the modified document showing previous and new wording and an explanation of the changes. If changes are widespread, a new version of the document should be provided instead. In CTIS, these documents can be placed in the placeholder 'for publication'. The version 'not for publication' is available to protect CCI or PPD as mentioned in article 81(4) of the Regulation. See also the Sponsor Handbook.
49.	Training & Support	What is the expected format and content of each notification? Which field/document is disclosed and when?	Information is available in the "CTIS Structured data form – Notifications" document, that is published in the Sponsor Handbook (7.1.2.). Refer to columns "Conformance" and "Publication" in the Excel file. The time when a notification will be public may depend on the trial category, information whether a field is deferrable or not has been included in column "Deferrable".
50.	Training & Support	Is there any technical support available on CTIS, e.g. online helpdesk or live chat?	Questions can be raised via the User Support Service through the CTIS webpage. No chat platform is foreseen.

Q. No.	Category	Question	Response
51.	Training & Support	Are there any templates available for the different types of documents that need to be uploaded in CTIS?	Templates including for Part II have been published on the EudraLex - Volume 10 - Clinical trials guidelines website. The development of further guidance and templates may be considered in the future.
52.	Training & Support	Can a sponsor (e.g. Investigator Initiated Trial sponsor) cross reference to another sponsor CTA IMPDs etc.?	There are provisions to enable sponsors to refer to another application. More details can be found in the EudraLex – Volume 10 Q&A, chapter III.
53.	Training & Support	Is there any specific training for GMO applications, e.g., for specific requirements in CTIS?	There is no specific training for GMO applications in relation to CTIS, as there are no specific requirements concerning GMO applications in the CTR. In practice, a sponsor needs to do one submission through CTIS, and one to each member state for the GMO aspects as applicable. GMO, radiopharmaceuticals, human tissues and cells, human blood and blood components, human organs intended for transplantation have dedicated legislation that would apply. See Article 91 of the CTR: "This regulation shall be without prejudice to Council Directive 97/43/Euratom, Council Directive 96/29/Euratom, Directive 2001/18/EC of the European Parliament and of the Council, Directive 2004/23/EC of the European Parliament and of the Council, Directive 2002/98/EC of the European Parliament and of the Council, Directive 2010/53/EC of the European Parliament and of the Council, and Directive 2009/41/EC of the European Parliament and of the Council."
54.	Training & Support	If in a given trial (trial B) no IMPD is submitted but reference is made to another trial (trial A) (with respective trial no. and justification in the placeholder IMPD of trial B), can the two trials run in disjunct countries? For example, trial A in Germany, Austria, and Belgium and trial B in France, Italy and Spain? Or is this option only possible for CTAs having the same RMS?	Reference can only be made to another trial in which a Member State was also the Member State Concerned. The IMPD of a trial authorised under the CTR by MSC 1, MSC 2 and MSC 3 can be referred to in another trial where these MSs are also concerned. The reference is not possible for Member States that are not concerned.

Q. No.	Category	Question	Response
55.	Training & Support	Is it possible to download from CTIS all editable data entries (filled in online in the editable fields of the FORM, Part I, Part II sections) into a PDF document for the different types of applications (Initial, Additional Member State Concerned Application, SM, Non-SM)? Is the download permission dependent on the user roles?	It is possible to download data and documents before and after submission. Users will get a zip folder containing the files of the CT, such as the documentation related to the evaluation of Part I and Part II of the initial application, the publication dates for data and documents. The structured data of the CT will be saved in PDF predefined templates. It is also possible to download in a PDF the 'evaluation' section, including RFI raised at the time of validation/assessment of Part I/Part II. See Training module 9 "Search, view and download information on clinical trials and clinical trial applications" and in the Sponsor Handbook. You can download information according to the view permissions mapped to your role. As a general rule, users are only able to retrieve CT and CTA information for those trials in which they are involved, and have been assigned a role to by an administrator within their organisation. The possibility to view and download CTs and CTAs data and documents is limited to the areas of action of each role assigned in CTIS. This means, for example, that a user that only has Assessor Part II preparer role, is not able to view or download Part I information of the CTA.

Q. No.	Category	Question	Response
56.	Transition Period	How can the sponsor get ready for CTIS during the transition period?	There is a 3-year transition period that started on 31 January 2022, on the CTIS go-live date. During the first year, sponsors could choose whether to apply for a new CTA under the Clinical Trial Directive (CTD: Directive 2001/20/EC) using EudraCT, or to apply under the new legislation (CTR: EU No 536/2014) using CTIS. From 31 January 2023 all new CTAs must be submitted under the new legislation (CTR) using CTIS. The date 30 January 2025 marks the end of the transition period, clinical trials cannot continue running under the old legislation (CTD) utilising EudraCT. If sponsors are running trials that are expected to continue beyond 30 January 2025, they will need to transition them to the CTR (CTIS) before the transition period expires. See also the following documents: • EudraLex – Volume 10 Q&A Chapter 11 - Arrangements for the transitional period • Clinical Trials Facilitation Group (CTFG) Best Practice Guide for sponsors of multinational clinical trials with different protocol versions approved in different Member States under Directive 2001/20/EC that will transition to Regulation (EU) No. 536/2014 • Sponsor Handbook
57.	Transition Period	In the last year of the 3-year transition period, do the sponsors need to transition all clinical trials that are still active at the time of the end of the transition period?	Transitioning to the CTR is only required for CTD trials which will have at least one site active in the EU on 30/01/2025. Trials authorised under the CTD that have the end of trial notified in all Member States (in line with the requirements of the CTD), will not need to be transitioned, even in the case when the global end of trial has not been reached yet. For CTD trials that do not transition to the CTR, the obligations for result reporting in EudraCT remain in place and accordingly, EudraCT will remain open for the submission of trial result summaries beyond 30/01/2025.

Q. No.	Category	Question	Response
58.	Transition Period	Will the labels need to be compliant for CTR Annex IV when an ongoing trial is transitioned to CTR? E.g. omission of expiry date on small primary packaging as permitted under current Directive.	See Question 11.9 in the EudraLex - Volume 10 Q&A document: When is a sponsor expected to update trial documents and labels? "The sponsor should bring documents related to the clinical trial in line with the CTR requirements (including the EUCT number) at the latest at the time of authorisation of the first Substantial Modification of a given document. For the labelling of IMP and AxMP, it is expected that the sponsor updates the label for those batches that are (re)labeled after the authorization under the CTR. There is no need to pro-actively relabel released IMPs."
59.	Transition Period	How do trials that may currently be authorised as a combination of interventional and non-interventional trials in different MSs need to be considered in light of CTR transition?	A trial that is transitioned needs to be submitted under the CTR to all MSs where the trial is still ongoing, independent of its status. During the validation phase, the RMS will determine whether the clinical trial applied for falls within the scope of the CTR (article 5(3)).
60.	Transparency	What is the requirement for the documents included in the CTA application that might contain PD or CCI? Is the applicant required to upload in CTIS both the complete document (RMS/MSC) "not for publication" for the purpose of assessment and the redacted/anonymised document "for publication" to fulfil public disclosure?	The document upload functionality enables to provide two documents, one "for publication" and one "not for publication". Only the version labelled ''for publication'' is published. This functionality aims to protect PD (if captured as needed) and CCI. Of note CCI can also be protected by the possibility to defer the publication of documents and structured data. Redaction of CCI and deferrals, should not be used simultaneously. Other documents, for example the ones containing information on quality or financial arrangements, will only have a 'not for publication' version. The EMA's CTIS training and support website makes reference to this information in the "overview" of each "CTIS Structured data form" excel file, where some relevant instructions have been included. See also the Sponsor Handbook.

Q. No.	Category	Question	Response
61.	Transparency	At which timepoint of the CTA assessment is the redaction of PD/CCI reviewed and accepted? Which authority is responsible for the review/approval? Who decides if the information is PD or CCI (Sponsor/RMS/EMA)?	Every party using CTIS is responsible for data protection when they are entering information in the system. Sponsor users need to bear in mind that the 'for publication' version of the documents will be published, therefore it is their responsibility to follow the GDPR for the PPD. Please consult the CTIS JCA for more information. CTIS will not validate PDF document author information, nor any other personal data that might be contained in the documents uploaded in CTIS. Any personal information provided in the document properties or in the content is governed by PPD rules applied to any CTIS content. CCI can be protected via means of redaction of what is considered CCI by the sponsor at the point in time when the documents are submitted through CTIS. CCI can also be protected by the possibility to defer the publication of documents and structured data. Redaction of CCI and deferrals should not be used simultaneously. See also the Sponsor Handbook.
62.	Transparency	At which timepoint of the CTA assessment is the deferral of public disclosure for some documents discussed/approved? Which authority is responsible for the review/approval? When does the sponsor get a response to a deferral request? How is a deferral on the ARs requested?	The proposal on deferrals made by the sponsors at the time of submission of an initial application will be reviewed by the RMS in conjunction with the MSC, as applicable, as soon as an application is submitted. Any consideration to the proposed trial category and deferral timelines may be communicated by the RMS in an RFI, at validation or most likely during Part I assessment. The deferrals on ARs and RFI can be defined by each MSC individually when issuing the decision on the CTA, as long as the sponsor has already requested a deferral to the protocol and the RFI response. The sponsor is not involved in the decision for the deferral of ARs, which is only selected by the MSC. It is expected that, in principle, the MSCs will apply the same timelines as the sponsors to delay the publication of their assessment reports (conclusion by RMS for

Q. No.	Category	Question	Response
			Part I, conclusion by MSCs on Part II, respectively) and RFIs sent to the sponsors.
63.	Transparency	Is the date of disclosure (depending on the deferral/study phase) be attached automatically to the redacted/anonymised document at the time of the CTA approval, and automatically made public when that date is reached?	Yes, in case of deferral, the 'for publication' version of the documents get automatically published in the CTIS public domain at the designated time. No manual intervention is needed by the user to trigger publication.
64.	Transparency	Is there any opportunity to amend the redacted/anonymised documents after the CTA approval, but before they are disclosed to the public?	Structured data and documents submitted via CTIS are publicly available according to the publication rules. The content of the documents provided in a CTA can only be modified during the application evaluation phase, by raising an RFI. After a decision is issued by the MSC on the application, it will no longer be possible for the sponsor to modify that application, even if the documents are not published yet due to deferral rules.
65.	Transparency	Some requirements of Policy 0070 and the CTR seem to differ, especially on the scope of the documents to be submitted. Is there any guidance regarding this?	Alignment on the publication of CSR and avoid duplication of efforts with policy 0070 is part of CTIS delivery plan. More information will be provided in a later stage.
66.	Transparency	Is it possible to request a deferral after the application was submitted? If so, would that be an NSM according to Article 81.9?	The request for a deferral should be done in the initial application. Once decided, the deferral set up applies to the current applications and to any subsequent applications and information provided by the sponsor during the lifecycle of the trial. During the assessment of the initial application, the RMS in conjunction with MSC may query, via an RFI, the deferral request, and the sponsor can adjust their deferral settings via their responses to the RFI. However, a change or an update to the deferral cannot take place via a SM or NSM.

Q. No.	Category	Question	Response
67.	Transparency	Article 37(8) of the CTR stipulates that the summary of results of an intermediate data analysis shall be submitted to the EU database within one year of the intermediate data analysis date. This means, the due date is not usually 12 months after the end of the trial as written below, but 12 months after the date of the intermediate data analysis. Is the below text from the Appendix document correct, i.e. can intermediate results really be deferred until 30 months after the end of the trial? Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited (EMA/42176/2014)", section: Clinical trial results summary for an intermediate data analysis states that should be made public in accordance with article 37(8).: "Sponsor may opt to defer the publication of the summary of results of an intermediate data analysis (if foreseen) in all or in part up to a maximum of 18 months after the due date (usually 12 months after the end of the trial unless article 37(4) applies) of the final summary of results and layperson summary (in total, a potential maximum of 30 months after the end of the trial) or until the time of MA if the time is earlier."	The text in the Appendix document is correct. Note that the deferral to publication of intermediate data analysis is part of the overall CTA evaluation process.

Q. No.	Category	Question	Response
68.	Transparency	Do listings need to be uploaded in a redacted way? For example, when CSRs contain pseudonymised (i.e., PD) in the subject listings.	Individual patient data listings are not expected to be submitted to the CTIS. Refer to section 4.7 of the Appendix on disclosures rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014": 1. CSRs, as submitted in marketing authorisation applications in the EU, or variation or line extension to these, including all appendices except those listing individual patient data, will be submitted to the database by the marketing authorisation applicant and made public within 30 days after the day the MA has been granted, the procedure for granting the marketing authorisation has been completed or the applicant has withdrawn the application. 2. The CSR report should be redacted/anonymised by the marketing-authorisation applicant before it is submitted to the database (see section 4.5 last paragraph).
69.	Transparency	What documents will be made public regarding Part II, especially if the templates put together and recommended by CTEG will not be used by the sponsor?	All documents 'for publication' provided in Part II, with the exception of the financial arrangements, will be published regardless of whether the templates recommended by the CTEG have been used. The Final AR Part II 'for publication" will also be published, regardless of the template/format that will be used.
70.	Transparency	Do the deferral rules also apply for paediatric trials or only for adult trials?	A deferral mechanism is applicable to each CTA, regardless of the population age. However, it should be noted, that for clinical trials in paediatric population or if the trial is part of a paediatric investigation plan (PIP) for a category 1 trial, e.g. first in human, BE/BA, bio similarity trial, it will not be possible to request a deferral for the following elements: • Main characteristics of the trial (trial title, inclusion /exclusion criteria, main objective, product details, etc.) • Notifications • Summary of results • Intermediate data analysis

Q. No.	Category	Question	Response
			More details can be found in Table 1 of the Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014"
71.	Transparency	If an information/document is made public by mistake, what's the process to get it removed from public view?	The removal of the document can be requested via the *Request removal of public information* link on the CTIS public website. The EMA removes the document if the request is valid. Documents cannot be removed from the public domain by sponsors or authorities, this function is only available to the EMA users.
72.	Transparency	If a Sponsor plans to conduct a Phase I/II clinical study but the trial does not progress to phase 2, is the trial still considered a category 2 trial for the purposes of data and document publication?	If the protocol combines several phases, e.g. I/II, the publication rules for the higher category (shorter deferral, by choosing category 2) should be selected by the sponsor, independent of when the actual Phase II part starts. See Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014"
73.	Transparency	Is there guidance available on which personal information should be redacted, for example in relation to the information considered PD within Part II documents relating to trial site staff, DSMB members, qualified persons, or other individuals not employed by the Sponsor?	The Draft guidance on PPD and CCI in CTIS is available on the EMA website. Information of PPD is also available in Training module 12. Please also consult CTIS data protection notice, annex II of the JCA for visibility of personal data included and published via CTIS. In principle, PD should not be available in the version of the documents 'for publication'. The only PD that should be available in the public domain are: • Details of the principal investigator • Details of the sponsor legal representative • Details of the head of institution testifying to the suitability of the facilities This is in line with the requirements of the Appendix on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014"

Q. No.	Category	Question	Response
74.	Transparency	Is there any specific guidance on the types of CCI that are considered acceptable for redaction within 'for publication' versions of documents submitted in a CTA?	The Draft guidance on PPD and CCI in CTIS is available on the EMA website. Information on PPD is also available in the Training module 12. The deferral mechanism has been included in CTIS to reduce the burden for sponsors on CCI redaction, therefore the protection of CCI in the documents should always be considered together with the deferral of publication applied, if any.
75.	Transparency	The redaction of the third country inspection reports is particularly challenging for Sponsors and CROs, as such reports can include both personal information and information relating to other trials that need to be submitted to CTIS separately (if within scope of the EU CTR). Will the expectations and principles of redaction for third country inspection reports be specified in any guidance that is planned?	Submission of third countries inspectorate inspection report should occur for each trial separately. If during the same inspection multiple trials have been inspected, then the same report can be provided in CTIS for each inspected trial. See the draft guidance on PPD and CCI in CTIS on the EMA website. Information of PPD is also available in Training module 12.
76.	Transparency	Which appendices of the CSR must be submitted within 30 days of MA? Should this be the in-scope Policy 0070 appendices or is it up to the sponsor to determine which appendices do not contain individual patient data and include those in the submission?	Refer to the Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited'': 4.7. CSR submitted by the marketing-authorisation applicant: 1. CSR, as submitted in marketing authorisation applications in the EU, or variation or line extension to these, including all appendices except those listing individual patient data, will be submitted to the database by the marketing authorisation applicant and made public within 30 days after the day the MA has been granted, the procedure for granting the MA been completed or the applicant has withdrawn the application. 2. The CSR should be redacted/anonymised by the marketing authorisation applicant before it is submitted to the database (see section 4.5 last paragraph).

Q. No.	Category	Question	Response
77.	Transparency	What are the requirements for deferral justifications (i.e. the justification published at the time of the decision and the justification published with the IB)? Is there specific information that should be included in the justification? Is there a character limit on deferral justifications? Under what circumstances may a MSC disagree with a sponsor's request for a deferral?	The RMS/MSC will consider during the assessment the categorisation of the trial and the justification(s) provided for the choice of deferral. It will be a case-by-case judgment, also taking into account the information that might already be available in the public domain for the trial/product documentation. The limitation for free text fields is 4000 characters. See also the Sponsor Handbook.
78.	Transparency	Trigger for publication of clinical data under CTR In accordance to Art. 37.4 of the CTR 'where the clinical trial was intended to be used for obtaining a marketing authorisation(MA) for the IMP, the applicant for marketing authorisation shall submit to the EU database the CSR within 30 days after the day the marketing authorisation has been granted, the procedure for granting the marketing authorisation has been completed, or the applicant for marketing authorisation has withdrawn the application'. Is the publication of CSRs to be triggered for any MA granted in EU (EMA, member states) upon CTR go live (any MA granted from 31 January 2022) or is the current hold on publication of clinical trial data (Policy 0070) to be prolonged in relation to EUCTR Art.37.4.?	The requirement for submission of CSR to CTIS only applies if the MA contains EU trials that were submitted in CTIS and authorised under the CTR. To the extent that the trigger for CSR publication in CTIS is reached that CSR would have to be published within 30 days after the end of the MA procedure. Alignment on the publication of CSR and avoid duplication of efforts with policy 0070 is part of CTIS delivery plan.
79.	User Management	Is there any guideline for sponsors on user management in CTIS? E.g. how to use the user management functionalities; how to manage user permissions and understand the user roles better?	User management is explained in the Sponsor Handbook.

Q. No.	Category	Question	Response
80.	User Management	Can a CRO request the Sponsor Admin role directly by submitting in EMA Account Management (IAM) a Letter of affiliation (Power of attorney / Letter of authorisation) signed by the sponsor (i.e., the sponsor does not have to register via IAM) or is the first Sponsor Admin role limited to the sponsor organisations?	The request for a first user to become Sponsor Admin for the sponsor organisation is managed by the EMA. It is not mandatory for the sponsor organisation to assign the role of the first Sponsor Admin to an internal employee. This role can be assigned to an external person (e.g. contractor). An individual can become the Sponsor Admin for an organisation by providing the valid documentation Letter of affiliation (Power of attorney / Letter of authorisation) signed by the sponsor. After this, all requests of other users to become a Sponsor Admin will be managed by the first Sponsor Admin in the IAM system. An affiliation letter is mandatory for the requests managed by the EMA. See also the Sponsor Handbook for more information.
81.	User Management	It is possible to have several Sponsor Admins, the first being validated outside CTIS, the following being assigned within CTIS. What happens if the validated Sponsor Admin (first CTIS Sponsor Admin) leaves the company? Does another validation need to take place?	All requests for the Sponsor Admin role are submitted and managed outside CTIS, in the IAM system. No such request is managed in CTIS. The first Sponsor Admin assigned in the IAM System by the EMA, on the basis of the validation of the request. The first Sponsor Admin will be able to handle further Sponsor Admin requests in the IAM System. It is possible to have more than one Sponsor Admin. Sponsors are encouraged to have at least two users with the Sponsor Admin role (for back-up reasons). If the first Sponsor Admin (or another user) leaves the company, one of the remaining Sponsor Admin needs to remove the role from the user's profile in IAM. There is no difference in functions between first Sponsor Admin and second/third Sponsor Admin, and each of them can remove the roles from the other users' profile. More details can be found in the EMA Account Management Training Session presentation slides. Users can also remove roles they have in their EMA Account and no validation is needed. EMA is not involved in such removal.

Q. No.	Category	Question	Response
			See also the Sponsor Handbook and EMA Account Management | Frequently Asked Questions FAQ number 13.
82.	User Management	If an individual consultant (self-employed) should take on a role on behalf of a sponsor company, what should the consultant enter as "Employer"? His/her own name?	The role to take on in CTIS and the entry concerning the employer depends on the contractual arrangements between the sponsor company and the individual consultant.