European Federation for Exploratory Medicines Development

EUFEMED Innovation Club Workshop: 16 September 2022

Submitting an application for a CTA and what do Sponsors from outside the EU need to consider

Summary

Under the clinical trial regulation (CTR), authorisation of the clinical trial application (CTA) has to occur through a new process: a single dossier has to be submitted to the one portal (EU Clinical Trial Information System [CTIS]). Sponsors have to respond within a few days to deficiencies in the validation process and to 'Requests for Further Information (RFIs)'. Access to CTIS, the dossier preparation and submission, and the decision-making process on further information to be submitted require a very detailed planning and agreement between the Sponsor and clinical trial unit/contract research organisations (CROs) on responsibilities and oversight.

In this webinar we will discuss strategies and first-hand experiences on efficient collaboration between international Sponsor organisations and early phase service providers.

Session moderator:

- Izaak den Daas; Director Patient Studies at QPS Netherlands BV

Expert panel:

- Seán Kilbride; Associate Director Regulatory Affairs at Regeneron Ireland
- Magaly Woolard; Head of Study Start Up at Regeneron Pharmaceuticals, Inc.
- Rishi Sarna; Associate Director Regulatory Operations at Regeneron
- Nina Berberich; Senior Manager Regulatory Affairs at MorphoSys
- Cynthia Lesbros; Head of Project Management in Clinical Research at Eurofins Optimed Clinical Research
- Mariska Beukers-Reuvers; Director Project Management at QIP Netherlands BV

Introduction

This meeting was introduced by the moderator, Izaak den Daas, and EUFEMED's President, Tim Hardman. This webinar was the second in the series on the new CTR coming into effect in 2023. Under the new CTR, all CTAs will be authorized after submitting a single dossier via a single system: the CTIS. With the new system, study Sponsors will be expected to respond to requests within a matter of days, which will considerably impact those located outside the EU. After introducing the various panellists, discussions began with an overview of

submitting a CTA and strategies on setting up efficient collaborations between international Sponsors and CROs.

Speakers: Seán Kilbride (Regeneron), Magaly Woolard and Rishi Sarna (Regeneron)

Background

Examining at the current procedures, the initial goal was to identify any gaps that were likely to arise under the new CTR. A pilot programme has been started to submit CTAs through CTIS. Currently in progress is the implementation of the findings from the pilot programme submissions and the goal will be to have full implementation in Q1 of 2023. Although there is transition period, the CTR will shortly become mandatory, and to implement these mandatory requirements, engagement of leadership (within Regeneron) in the EU and in the US was necessary.

CTA: Part One and Part Two – Overiew

Under the single CTA submitted via the CTIS portal, there are two parts to the dossier. Part One is the scientific and technical documents (e.g., protocol, Investigator's Brochure, Investigational Medicinal Product Dossier [IMPD]) and it will be assessed by single member states (irrespective of the number of member states involved), which will generate a single Part One assessment and a single Part One conclusion that will cover all member states.

Part Two is conducted by each member state that will be reviewed at a member state level. Based on current experiences, the feedback has been at a member state level instead of the national competent authorities (NCAs) or ethics committees (ECs) level. Thus in the end, there is one decision per member state per procedure.

The Role of an International Sponsor

Regeneron is in a unique position in that its headquarters are based in the US and it is the Sponsor for all of the studies in Europe. As this dynamic will continue under the CTR, the regulatory affairs team has been instrumental in preparing those in the US to implement the new regulation. To fully prepare for the CTR, those involved in the effort included teams from regulatory affairs, clinical trial management, study start up, transparencies, safety and study templates, vendor management.

The Role of CROs: Multinational Submissions

Under the new directive, for Part Two, there will be heavy reliance on CROs; although some aspects of the regulation will allow some work be performed "in-house" rather than using CROs. For instance, the regulatory affairs division will be the legal representation for the CTA. While previous distributions were to the NCA, under the new CTR, the EU regulatory team was able to lead the submissions and pull documentation together to submit Part One. When submitting CTAs within Regeneron, the clinical team led ethics submissions and

responses under the new CTR. Going forward, the study start up team will be responsible for submissions and responses to requests for further information. This approach only worked for single-site studies and where there were local offices (such as Ireland and the UK), and for some multinational studies depending on the location (Belgium). For multinational studies in the EU, CROs were used for those national submissions as well as for local additional requirements or translations. Of note, Regeneron has some experience submitting multinational clinical trials under the voluntary harmonisation procedure (VHP) under the directive.

Part One Requirements

As an example, Part One can be divided into three sections. The medical writing team put together the protocol and IB in one section, the CMC team put together the IMPD and GMP documents, and the label came from the clinical drug supply team.

There are notable differences compared to VHP under the new CTR. These include:

- Protocol synopsis
- Registering products and third-party vendors before submission (European Medicines Agency [EMA] substances, products, organisations and referentials [SPOR] database, etc.)
    - Data privacy statement – states compliance with General Data Protection Regulation (GDPR) and local data privacy laws
- Translations (outlined for Part One documents on the European Commission website)
- Redactions and transparencies
    1. Redact documents
    2. Deferrals on categorising different studies by phase

Part Two Requirements – Speaker: Magaly Woolard

Part Two, also referred to as the 'Member State Requirements', as at the country level, it will be the member states that determine what ECs will be identified to preside over the review and approval of the clinical trial. The CTIS portal requires that Sponsors select the institutions or organisations from an existing database or repository; therefore, self-registering in advance of participation in a clinical trial is required to avoid delays.

Required standardised documents include the following:

- Curriculum vitae
- Medical licenses
- Site suitability assessments
- Conflict of interests
- Any additional data privacy requirements

- A master agreement/contract with each site's trial insurance
- Consent forms
- Any recruitment compensation materials
- Guidance on collection and use of biospecimens
- Translations, redactions, and/or deferrals

After the Submission

Once documents are submitted to each member state, requests for information or queries by the member state and/or identified ECs may be returned. Once triggered, there are 12 calendar days to respond to these requests.

For member state approval, it is a consolidation of help authority and EC approvals. Once all documentation is in place, the Sponsor issues notifications to all health authorities and corresponding ECs with study and country level event dates for the following events: starting the trial, initiating enrolment, completing enrolment, completing the trial, and if the study or enrolment has been put on hold, restarted, or if early termination is being considered. Notifications have to be completed or reported within 15 calendar days. Sponsors will also have to issue notifications if sites are added to the trial or if any primary investigators change during the conduct of the study.

In the CTIS, a date has to be forecasted for when the study results will be generated, that is, after distributing the approved Clinical Study Report (CSR) and providing any end of study media in support of the CSR.

Submitting to the CTIS Portal – Rishi Sarna

The CTIS portal has been active since January 2022. It is the single point of entry for clinical trial information in Europe. The portal enables the electronic exchange of information between the Sponsor and authorities, which will hopefully lead to an increase in safety and transparency. There are three main areas in the CTIS:

- The ***Sponsor workspace*** enables Sponsors to submit applications, trial events and report other events during the lifecycle of the clinical trial
- The ***authority workspace*** allows each member state and European Commission to assess and oversee clinical trial information
- The ***public portal*** allows the general public to view information related to clinical trials

CTIS Master Trainer

The CTIS master trainers are a core group of approximately 150 users across Europe. The trainers pass on information through their company in a streamlined, top-down approach. The EMA adopted this approach instead of setting up multiple webinars and conferences. Only one CTIS Master Trainer per organisation was permitted. These trainers serve as the

main point of contact with the EMA in which they received updates and training materials (32 hours of training). Responsibilities of the trainers include ensuring that future CTIS users within their company are fully prepared to submit a CTA.

CTIS Portal Access

Although there a number of ways to set up the CTIS portal, within Regeneron, a role-base system for managing access was used to ensure that the right people with the correct level of access. For the portal itself, an organisation-centric approach is recommended by the EMA. Under this setup, a high-level Sponsor admin, who is validated by EMA, would manage the access of and approve users who would then become affiliated with the organisation of the Sponsor. To create a clinical trial, the CTA would need to be approved by the Sponsor admin. Through this approach, there is a layer of security as only admins could create clinical trials; moreover, it provides a central point to manage access, which is helpful when working with external parties.

Once a trial is created, within Regeneron there are four active teams that would populate components in the portal:

- ***Regulatory Liaisons*** and ***Study Start Up Teams*** – perform the role of clinical admin, they are responsible for creating, populating and submitting trial information, responding to RFIs and submitting notifications
- ***Clinical Trial Transparency Team*** – monitor system for alerts and notifications and submit end of trial results
- ***Regulatory Publishing Team*** – submits annual safety reports

Training Users on the CTIS Portal

To train colleagues on submitting and interacting with the CTIS portal, a combination of four methods is used. First, users are assigned procedural documentation to read and understand before obtaining access. Next, a web-based curriculum is assigned to users, depending on their future role in the system. Completion of the online training is required before a role can be requested in the CTIS. While users have access to the CTIS portal, a series of how-to videos are provided in which the videos can be watched at any time, including when simultaneously carrying out tasks in the portal. Finally, there is the CTIS 'sandbox', which enables users to practice populating and submitting dummy information, thereby allowing users to fully familiarise themselves with the portal.

Experiences in Submitting CTAs – Speaker: Seán Kilbride

First Application: New CTA in Belgium

This new CTA application was for a minor national study in Belgium in which a standard monoclonal antibody was used. As the submission was for one country, an enhanced

submission was used. The study was initially submitted 28 July 2022 and validated with no issues on 01 August 2022. As a monoclonal antibody was used, the reporting member state requested additional time (25 days) for an assessment of Part One to consult with an external committee. When the agency was contacted, the Belgian authority stated that although they requested a set amount of time, they would not use the entire time, which was the case. On Day 36, RFIs for Part One was received (07 September 2022), and on Day 45, RFIs for Part Two was received (15 September 2022). As 12 days are allowed for responses to RFIs, responses to Part One was submitted on 16 September 2022. During this process, the member states asked for a Protocol Amendment, which had to be submitted within the 12-day turnaround time along with responses to RFIs.

Frustratingly, RFIs disappeared from the CTIS after they were received, which could make it difficult to respond to the requests and keep the procedure open. This issue has been raised as a bug with the EMA and Belgian authority.

Second Application: Existing Mononational Study

As the Phase III study is already running and has been scheduled to continue through January 2025, we took the opportunity to gain experience and transition this study early. On 05 August 2022, no new documents were generated, only the bare documents that had been approved under the new CTR were submitted. Some validation queries were addressed. Conclusions for Parts One and Two were received the week of 12 September 2022, and a positive decision was received on 16 September 2022.

Lessons Learned during Pilot Programme

After going through a few submissions and using templates from the EMA and the European Commission, we have updated/modified the following documents:

- Protocol
- Protocol synopsis – lay language/summary requirements
- Investigator's Brochure
- Label – complies with EU CTR
- Translations and redactions – processes have been set up in-house and with external CROs
  NOTE: All new CTAs must be redacted
- Summary of results upon study completion
- Translations in CTIS portal (country-dependent), additional documents to be uploaded

Role of CROs for Part Two – Speaker: Magaly Woolard

Partnering with a number of CROs has been helpful in capitalising on their country-specific experiences and managing day-to-day activities. For multinational large Phase II and III

studies, the appropriate documentation has been put in place to clarify the roles and responsibilities of CROs that partner with Regeneron. Additionally, a regulatory network responsibility assignment (RACI) chart has been introduced which identifies who is accountable, responsible, consulted and/or informed for any step in the process. Any CRO or vendors that work with Regeneron are required to pre-register in the CTIS database; therefore these external companies can be identified from a notification/delegation of responsibility point of view. Currently, there are a number of pilot studies where CROs are acting on behalf of Regeneron.

Positives and Negatives of the CTIS Portal – Speaker: Rishi Sarna

Positives

- Created a streamline approach for creating clinical trials that is working well
- Frequent communication and collaborations amongst teams
- Management access acts as a backup for peers
- Additional project management and publishing support to help with submissions in CTIS
- Exposure to the system via the CTIS 'sandbox' has helped with training

Negatives

- No email notifications; the system has to be constantly monitored to capture alerts or RFIs
- First version of a document is automatically published – choosing the redacted version is key
- Renaming documents to ensure date and version match document is time consuming
- Technical difficulties encountered on the day of submission; future goal is to submit a day or two in advance if possible
- The size limit of a document is 10 megabytes (MB) – documents have to be shrunk or split
- Products and substances need to be registered in the database in advance (process takes 2 days for items to show up in the CTIS portal)
- The EMA Help Desk is often slow in responding even when the ticket is marked as urgent (example: disappearing RFIs)

Discussions

Following the presentation, a panel discussion was held and moderated by Izaak den Daas. Each panellist gave a description of their credentials and their professional involvement in the implementing the new CTR.

Izaak den Daas initiated discussion on several topics, and the audience were also asked to submit questions to the panel of experts to feed discussion.

Questions (Q) from the audience are outlined below as are the individual speakers for each answer.

Q: For a monocentric, Phase I study in Belgium, the timeline for approval is 20 days – is that correct?

Seán Kilbride: That is what we originally applied for, although that was not our experience with Belgium. They told us for Part One that they would need an additional 25 days on top of the 45 days that they were already allowed. Perhaps in the future, it could be reduced to 20 days. But in our case for our study, it was 23 days when they sent us the request for further information for Part One, and then it was a week later before we received Part Two.

Q: When responding to an RFI the documentation is automatically considered for publication – can we change that?

Nina Berberich: I think this is not possible. You can apply for a deferral, at least for some specific categories. For Phase I trials, the deferral can last up to 7 years, but in the end, the data will be made public.

Seán Kilbride: A redacted document could also be uploaded. A trick of the system is that for every document you upload, the first document is published, but then there is a little '+' sign that can be clicked and you can upload a corresponding document that is redacted. That applies for both Part One and Part Two. There is an EMA video on how to upload redacted documents and unredacted documents to learn more.

Q: Regarding legal representation status, some member states require that you have an EU legal representative, but some only a contact person. Is there any information available on if this being harmonised? Would this be submitted with Part One or Part Two?

Seán Kilbride: There are at least five different contacts now required with the CTIS. It is under the form set, under the Part One section, and it is now part of the application effectively. In addition to the legal representative, there is an EU contact person that I think covers those countries that do not require a legal representative. In Regeneron, for the Dublin office, the legal representative is also the EU contact. There is also a Sponsor contact that is required and a public contact point. All of those details must be worked out before submitting a CTA, bearing in mind that from a company perspective, we are not naming people – rather we are protecting people internally. As all of this information is published, instead of giving an individual's name, we have given the names of the roles from within the company and corresponding emails for those roles.

Q: Which responsibilities in the trial approval process do you foresee for the Sponsor and the Phase I CRO in the first CTA for authorization, and later on as a routine?

Seán Kilbride: Our model for a mononational study, is if it is in-house, there is some strategy that has to be worked out. It depends on our capabilities in house. But if it is a mononational, monocentric study, we are going to try and submit those in-house under the regulation where possible. If it is beyond our resources, we will be asking CROs to submit the Part Two and prepare some of those documents together.

Nina Berberich: This question cannot be answered in general. Each Sponsor is organised differently. It is important to find a jointly-agreed operating model. It starts with the questions, "Who will get access? Which role should be assigned to a specific person? Who will organise the documents for Part One and Part Two? Who will manage the RFIs and endless required modifications?" There are many questions that must be aligned with the CROs and also within the Sponsor.

Q: Mariksa, you are dealing a lot with small customers and large regulatory departments – how are you dealing with that?

Mariska Beukers-Reuvers: For each study, we need a full, dedicated transfer of obligation and responsibility. It should be really clear split of who's doing what and the need for, like it was presented today and I think for Big Pharma, it is they have an in-house that they do themselves and they are quite prepared, I would say well prepared. But we work a lot with small biotechs, so they fully dedicated most of the cases to us as CROs, so then you have a different situation. We should be prepared for both situations. It should be really clear in the responsibility split who is doing what, and especially with a new situation (CTA) that should be really clear. And there is not a general answer, because it really depends on what the Sponsor is having in-house, i.e., what they're doing themselves.

On the other hand, as I just mentioned, we have very good collaborations with our local ethical board who will actually do the review. And they have specific, although it's a system used within Europe, they have specific some requests that we still have to adhere to. So I think, to still be in contact with the CRO or the site, just to make sure that even when, like in this case, today, you do it by yourself as a Sponsor, you still have maybe some specifics. So that should be really transferred then to the Sponsor, in this case, they are really making sure that they adhere to the specifics of the ethics board in this case.

Cynthia Lesbros: Regarding the small biotechs, we are thinking of organising some training as they have never used the CTIS, and they do not have time or resources to do the training by themselves.

Mariska Beukers-Reuvers: In addition to that, I think there is also a huge difference between Sponsors located in the European countries compared with US-based Sponsors, they are not well prepared I would say.

Izaak den Daas: Yeah, they are not realising there is a centralised system now in Europe, there is also a local situation as well. For instance, in the Netherlands, which is quite a different system than most other countries where the IRP is the same as the EC. And there was a NCA who is always now in place for getting the files from the central portal. For Phase I, they send it to the well-known Phase I EC. That system is actually more or less still in place. I think in the other countries, it is actually the same with a central portal and a cycle system. But also the local system has been adapted to that. And for American companies, it is not really comprehensible.

Q: How is your company (Regeneron), which is fundamentally an American company, how are they looking at this idea of this movement in a clinical trial regulation system?

Seán Kilbride: We are lucky to have offices in Dublin and in the UK. Rishi, our master trainer, is based in the UK. I think that we might be a different situation; additionally, we've successfully submitted if a couple of CTAs with a handful of requests for further information. There are advantages, such as the single assessment of Part One is being seen as an advantage, and the fact that we will not to present and amend the protocol multiple times for different authorities, which is really seen as a major advantage. Moreover, there are certainties with the timelines as well, particularly around interactions with ECs, which is a big advantage. The transparency is something that sent shockwaves through the company, but you know, as it has been mentioned in the questions and answers, there are deferrals in place as well for most documents and we are applying for those as well as redacting documents that are uploaded for publication. Thus, we were able to mitigate at least that major impact from the transparency side.

Q: There has been some discussion that about competition – is this a threat? or is it a blessing? Are we still in good competition with the US? Or are we losing? How are we losing out over here, and is this actually the same for the UK, which is also the third country and is not in the EU anymore? Any ideas to bring about how they are in the UK look at this European initiative?

Tim Hardman: It is very sad what is happening in the UK at the moment. I guess in the Phase I community, they are feeling as though they have got a lucky escape maybe. But I don't think that that is going to change or make us any way more competitive in the long run. I think we are in an international business and I think this certainly is the way forward in Europe, and I think maybe we missed a trick in the UK by not being involved in that. I am very sad about it to be honest.

Magaly Woolard: From my perspective, I feel there is tremendous benefit and driving towards standardisation. It makes the work much more repeatable and predictable and quite frankly, it brings a scale to the process when you know that all you have to do one thing, five times, seven times, nine times, as opposed to each interaction becoming very unique and distinctive. What I will say maybe is the challenge in this particular calendar year is that we are still encountering some resistance from certain countries, saying that they are

not ready to make the leap and to embrace the EU CTR. And what that forces the Sponsors to have to do is to get into more detailed and time consuming discussions to try to bring the country back on board with where EU CTR is going for those studies, whereas we at Regeneron have elected to align with EU CTR earlier. And I do not want to mention the countries in particular, but we are having to serpentine through some discussions about data privacy and do certain countries require more than what the EU CTR is going to be requiring. We are also navigating proof-of-payment, and who is requiring it and who is not now that EDI CTR is coming forward. How do we handle the generation and processing of that documentation? Because some countries still require payment before we submit, and others generate the proof-of-payment after we submit. And would it be lovely if that process could also have been standardised under the auspices of the EU CTR and share some of those examples and say there are still some hurdles that we are preparing for, and determine how we can clear them without compromising time. Hopefully those examples resonate for people.

Seán Kilbride: I will just add one more example because this is something that has generated a lot of discussion within Regeneron. Regeneron is a very innovative company, we have a lot of early products in the pipeline, we work with collaborators a lot and what the EU CTIS forces us to do now is share our IMPDs with collaborators. Because once a Sponsor is setting up a study in CTIS, they have full overview of the whole package. Previously, we could submit directly and IMPD to the member state and in the US they have this concept of a drug master file right at the IND level so they can protect the information that is most critical to their business. But the EMA has not facilitated that in the CTIS, and that will have a major impact on our collaborations for sure, with academic sponsors and with commercial sponsors. So it remains to be seen whether the functionality will change in relation to that, but at the moment, it looks unlikely that we will do collaborative studies where we will have to share IMPD with Sponsors where we would not have shared that before.

Izaak den Daas: The main aim for the EU CTR is of course harmonisation. If you think about doing a trial in six European countries, they would have to go to every board independently for getting permission, etc. The idea of course of getting this centralised is probably not a bad idea, but the proof of eating is in the pudding. We are still very early, but I think that in time, let's say in a couple of years, we will know more about how a clinical trial will look in different countries, as we will gain experience.

Q: Mariska, for a single country, single trial as most of the Phase I CROs have, is it slightly more complicated but not that much we can adapt to that. Is that a fair statement?

Mariska Beukers-Reuvers: I would say yes.

Do you see for a Sponsor in a Phase I CRO in the training needs – is that changed? How are we adapting to dates?

Seán Kilbride: Rishi, maybe do you want to take this one? because primarily, most of the training, I think has been in relation to the use of CTIS and the access management within CTIS.

Rishi Sarna: As I mentioned earlier, we there is a CTR master training initiative. So one member per organisation is invited to the training courses, and they must cascade information down. But the EMA has got a very good list of training material, they have got weekly videos. It is an online training tool that is split up by module. And that has been really key for Regeneron in using those types of training materials, and we have adapted some of those training materials. We have created our own how-to videos with the use of the 'sandbox', so there is a lot out there in terms of training and it is all on the EMA's website.

Q: Are there any comments, more foresight?

Nina Berberich: I think both Sponsor and CRO must be trained properly. I think there is no difference in the training materials, and also how to train the persons using CTIS. We have experiences with CROs that were not well trained and we had the impression that I had to train the CRO. Yeah, I hope that it will get better in the next couple of weeks, months, that the CROs are very well trained.

Q: From the CRO's side, any views on the training needs in this new system?

Mariska Beukers-Reuvers: I agree. We spent the last couple of months specifically on training. I agree with you that both Sponsor and CRO should be well trained and should be knowing everything about the new system. As mentioned before, from a CRO perspective, it is really important to agree with the Sponsor upfront of who is doing what. If, for example, in this case, the Sponsor is doing the full submission of Part One and Part Two, then there is less work for the CRO, on the other end, from a CRO perspective, we also work with small biotech. So there, I expect fully transparent, transfer to us and that CROs to know the full submission. From a CRO perspective, I agree we should be well prepared, because we kind of have both options, either full submission managed by Sponsor, or full submission by CROs. So we should be well prepared and trained for whole package, I would say.

Q: You put it in a document, didn't you?

Mariska Beukers-Reuvers: Yes, I think Seán has it in the beginning of the slides. We prepared a change control document. We need what is the process of who should be trained, trained in what, but also risk mitigation, pilot studies. Also, once the pilot studies are performed, learn from that experience. I saw some feedback in the comments. We have both procedures next to each other, still the old procedure because we have a transfer period of a couple of years. We have both processes next to each other. That is what we created. I think it is in line with the slide Seán had in the beginning.

Magaly Woolard: I will also share that we at Regeneron are a little bit reticent to try to restate everything that is already captured on the EMA website. There is extensive content there. And maybe to the earlier question there. There are nuances between Phase I studies healthy volunteers as compared to Phase II and Phase III. And I guess, my one suggestion, which is something that I am still trying to personally do, is to log into the EMA website at least once a month to try to review, consume and appreciate and master the guidance that is being given and the updates over time. But I think this calendar year, it has been really challenging to try to keep pace with all of the emerging documentation. Nevermind, compare, alright, what changed from the last time? A lot of healthy reading to be done? Maybe a weekend reading or evening reading, but I know it is hard to fit in with everything else that we need to do at a professional and personal level.

Q: Cynthia, I know you have had your company, Eurofins, has not been dealing with the new CTR due to conservatism of your clients. But generally, the clock is ticking, I would say, generally, do you have to do with any comments on what you hear right now?

Cynthia Lesbros: The next submission will be done with the CTIS because now they do not have another choice finally. It is not better, for example, we were ready to start meeting in June. But last time, the Sponsor did not want to go on. Regarding the training, I totally agree that all the videos and the training that are on the EMA site are very, very good and useful. Again, for the small biotechs, and so on, I think they are going to need, let's say, a special and very small training because they are not going to see all the videos to submit one study because both are going to have access. So then there needs to be training, otherwise, they risk that they have many, many questions.

Vicki: Yes, we need to, I think we have to discuss in a month with them because it is true for little biotech is that is a major point to check with them and to advise them is regarding the registration of the molecule in the EMA database, which can take some few weeks. And we have to take into account the delay of submission and so on.

Abbreviations

Abbreviation	Definition
CTA	Clinical Trial Application
CTIS	Clinical Trial Information System
CRO	Clinical Research Organisation
CSR	Clinical Study Report
CTR	Clinical Trial Regulation
EC	Ethics Committee
EMA	European Medicines Agency
EU	European Union
GDPR	General Data Protection Regulation
IMPD	Investigational Medicinal Product Dossier
IND	Investigational New Drug
NCA	National Competent Authority
RACI	Regulatory Network Responsibility Assignment
RFI	Request for Further Information
SPOR	Substances, Products, Organisations and Referentials