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Straightforward But Technical: Transferring Existing Studies To EU Clinical Trial Portal

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Executive Summary

At a webinar organized by the European Medicines Agency, EU member states discussed their experiences with reviewing the requests made by trial sponsors to switch existing studies to the Clinical Trial Regulation.

STUDIES AUTHORIZED UNDER CLINICAL TRIAL REGULATION BENEFIT FROM INCREASED TRANSPARENCY

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Although there is plenty of time until the 31 January 2025 deadline for ensuring that ongoing trials in the EU that were approved under the Clinical Trials Directive (CTD) comply with the Clinical Trial Regulation (CTR), sponsors are being urged to plan early for this making this switch.

The procedure for transitioning a trial from the CTD to the CTR is quite straightforward but "rather technical by nature," said Outi Konttinen, of Finland's National Committee on Medical Research Ethics, Tukija.

It requires sponsors to submit a new two-part trial application (relying on the existing dossier already assessed under the CTD and authorized by the member states) to the Clinical Trial Information System (CTIS) that became functional on 31 January 2022 to support the provisions of the CTR. (Also see "Here At Last: A New Era For Clinical Trials In The EU" - Pink Sheet, 31 Jan, 2022.)

Konttinen, general secretary and group leader at Tukija, was speaking at a virtual webinar organized by the European Medicines Agency on 1 July to discuss stakeholder experience with the CTIS. Delegates at the webinar were advised to plan early for submitting transition requests.

Finland took 23 days to authorize its first transition trial on 22 June, she said, explaining that the request for the switch into the CTIS had been submitted by the Turku University Central Hospital on 30 May. "Based on that experience, we know that the process [for authorizing transitional trials] can be much faster," said Konttinen.

Austria's first experience with a transition trial was more complex and took longer, according to Stefan Strasser, head of clinical trials at the Austrian medicines regulator BASG/AGES. The transition request was for a "very large and complicated trial" that put the best practices for transition to the test, Strasser said at the webinar.

The trial "needed three attempts to transition" so "maybe [it was] not the perfect pilot," he noted. The transition request was for EU-SolidAct, a randomized, multifactorial, adaptive platform trial for COVID-19 and emerging infectious diseases and pandemics. The trial was submitted to the CTIS on 15 March and was authorized by the 14 member states concerned (MSCs) at different dates, with Austria authorizing it on 25 May.

A key factor that contributed to the long transition timeline for EU-SolidAct was the fact that its sponsor, Oslo University Hospital, had not completely harmonized the trial under the CTD "and this is definitely what you should do" before submitting a transition request, Strasser explained. "It's in the best practice to do that," he added.

The transitioning of the EU-SolidAct trial was also a learning experience for Austria. The country's regulators want all authorized documents uploaded [into the CTIS] at the time of transition. Strasser noted that this may be contradictory to what was being advised in the European Commission's CTR Q&A guideline, but "now that we see how it really looks and feels," this advice may be changed.

Also for transition trials, Austria wants sponsors to ensure that all CTIS documents have the "right metadata, right name, right version" and to "check between the CTIS documents and the national documents" as the only assessment for such trials is done when the application submitted to the CTIS is being validated. There is no re-assessment of the trial submitted for transition.

Austria is currently dealing with another transition request. This request is by Promethera Therapeutics for its Phase IIb DHELIVER study to test the advanced cell therapy medicinal product, HepaStem, in patients with acute-on-chronic liver failure. The trial was submitted to the CTIS on 10 May. As of 26 July, it was

authorized in four of the 14 member states concerned, and it remains under evaluation in the remaining countries, including Austria.

While the commission has issued detailed guidance on transitioning trials from the CTD to the CTR, "we do receive some questions" on this topic, Monique Al, of the Netherlands' Central Committee on Research Involving Human Subjects (CCMO), said at the webinar. She highlighted the following factors for sponsors to consider:

> Only active clinical trials without any pending/ongoing assessment by regulators in any of the EU/European Economic Area (EEA) countries are eligible for a switch. "So, if you have a substantial modification still under review… [or] if your clinical trial is on hold in a member state, you can't transfer your trial," explained Al.
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> Only a trial that complies with the CTR as regards its substantial requirements can be transitioned. "It's the sponsor's responsibility to assess compliance to the CTR," Al said. If a trial does not comply with the CTR, a sponsor can request a substantial amendment under the CTD specifying their intention to align the trial with the CTR.
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> To transition a multinational clinical trial, sponsors will need a harmonized or at least a consolidated protocol. Al explained that a harmonized protocol is one that is "completely identical in every member state concerned," which means "everybody has the same version, date and content." As for the consolidated version, she explained, this refers to protocols that are not completely identical in all of the MSCs, but have the same core information.
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> For multinational trials, a transition request can only be submitted to those member states concerned where the trial is ongoing. "If you want to add a new member state [concerned] to the clinical trial, you can only do it after the transition" is complete, Al said.

The commission has specified in its Q&A CTR guideline which documents sponsors must provide to support Part I of their CTIS application. Al said that discussions were ongoing about this list "so please be aware that it might be updated."