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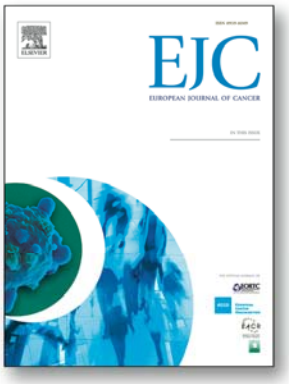

SUMMER 2014

Two cheers for the new Clinical Trials Regulation

In May 2014, the European Parliament voted overwhelming in favour of a new law, the Clinical Trials Regulation (2012/0192 (COD), which replaces the Clinical Trials Directive of 2001. The new Regulation, scheduled to take effect from 2016, has been widely welcomed because it streamlines the trial application process, distinguishes between low- and high- intervention trials and allows patients to give consent once for their data to be used beyond a trial. But the Regulation makes no provision for a harmonised patient insurance scheme.

The Clinical Trials Regulation was welcomed by the European Society for Paediatric Oncology (SIOPE) which has campaigned hard for the 2001 Directive to be amended. The new Regulation is a “major step forward”, according to Gilles Vassal, President of SIOPE. Under the Regulation, there will be a single point of submission – a European Medicines Agency portal – for all trial applications. “We have struggled during the last 10 years, trying to implement our clinical trials in paediatric cancer which need to be multinational while faced with all the disparities in interpretation [of the Directive] between one member state and another,” Vassal said.

ESMO has also greeted the new Regulation with enthusiasm. Jean Yves Blay, a member of ESMO’s Public Affairs Committee, agreed that the new Regulation will allow European cancer researchers to work to together more effectively. “Having a centralised application procedure and then a review by the member states is something that goes in the right direction. And it ensures that we as Europeans remain competitive and able to work together more efficiently.”

Françoise Meunier, Director General of the EORTC, while delighted that the new Regulation has been passed, remained concerned that there is no fixed date for the implementation of the EMA portal. Blay added that it is not completely clear how the two-step application process will work, and how traditionally slow and fast member states would respond.

“As researchers, we need to look at the true effects of this revision on the time to [trial] activation. This is a key issue – and we need to see if it meets the expectation of researchers and of patients.” Blay said.

A second positive aspect of the new Regulation is its differentiation between low and high intervention trials. Vassal: “The Directive was very much aimed at drug development trials for pharmaceuticals companies; the new Regulation, with two types of intervention levels, will really help us to better meet the needs of our patients – and not have a one size fits all situation and the administrative burden associated with this.

“We believe that this will facilitate the implementation of academic research trials trying to combine treatment strategies to improve the cure rate and to de-escalate the intensity of the treatment in those who would be cured – but who are at risk of sequelae in the long-term.”

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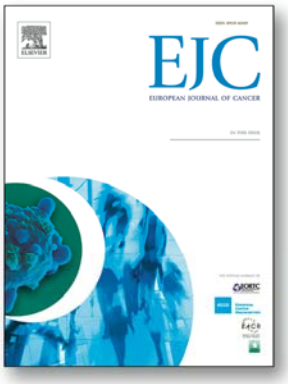

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A remaining concern, though, is the scope within the Regulation for different interpretations by member states of what constitutes a low intervention trial. Vassal believes this could lead to individual member states opting out of a multinational trial, and while this may not block a trial, it could severely hinder progress.

A third major plus point of the Regulation, according to ESMO, is its acknowledgement of the importance of using data stored by a clinical trial beyond the end of the study. It means that when patients consent to a clinical trial, they can also give a one-time consent for data to be used beyond the trial for medical research (they can withdraw this consent at any time). ESMO President Rolf Stahel said, "The concept of a one-time consent is an essential component of successful medical research."

> ***'We need to look at the true effects of this revision on the time to trial activation to see if it meets expectations'***
>
> **Jean-Yves Blay**
> **ESMO**

So far, so good. However, the new Regulation makes no provision for a harmonised patient insurance scheme. Vassal said, "We very much hoped a no-fault indemnity scheme for patients would be included but this was not approved. Our pan-European insurance costs will therefore remain extremely high."

Meunier is also disappointed by the lack of a legal requirement for a harmonised patient indemnity system. "It would have been simpler for each country to take responsibility for this with a no fault fund that could indemnify any damage to a patient participating in a trial." In Belgium, she said there was now such a scheme, which made it easier for patients to be protected, and this resulted in a lower administrative burden and insurance costs for trial sponsors.

Elsewhere, academic oncology trial sponsors will continue to face the growing problem of requests from local ethics committees about patient indemnification certificates which are not harmonised across member states. "This complicates the job of the sponsor because they have to fulfill all their requests for the same patients in the same trial," she said. "It is terribly cumbersome and also for me it is unethical to have different requests for the same risks for the same category of patient who are treated in the same way. The life of a patient in The Netherlands, Germany, France or the UK should be indemnified under the same scheme."

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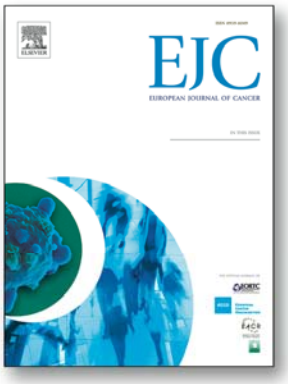

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The current insurance system results in a 7-fold difference in the rate per patient of insurance between member states, Meunier said.

Anastassia Negrouk, Head of International Regulatory and Intergroup Unit at EORTC, is concerned that some countries in multinational trials are making it a requirement that trial sponsors need to provide site-specific insurance certificates for each trial.

"This is just a requirement by a local ethics committee, it has nothing to do with the essence of any damage compensation involved," she said. "It adds to the costs and makes insurance very expensive for academic sponsors who cannot gain the advantageous global insurance rates negotiated by Industry trial sponsors."

Insurance costs for the average international trial now costs three hundred thousand to five hundred thousand Euros, "about the current total costs of a small non-drug therapeutic trial," she said.

Rising insurance costs disproportionately threaten trials into rare cancers, which by definition need international co-operation. "The insurance broker minimum price is for 10 patients. So if you want to include countries with rare diseases where you would only expect maybe 5 patients you still have to pay the price for 10," Negrouk said.

"We [the EORTC] have our ways, our mechanisms of helping. But I know that some smaller academic groups are really struggling to find this money," she said.

> ***'The lack of a harmonised no-fault indemnity scheme is disappointing, especially considering the amount of public money invested in health research, only for vast quantities to be handed to insurance companies'***
>
> **Glenis Willmott MEP**

Glenis Willmott MEP was the European Parliament rapporteur for the Clinical Trial Regulation and was responsible for steering it through. She said that every effort was made to try and achieve agreement on a harmonised no fault indemnity scheme.

"Despite giving Member States several different options on how the scheme could operate and be funded, the Council made it clear that it was not something they could accept in any form. This is disappointing, especially considering the amount of public

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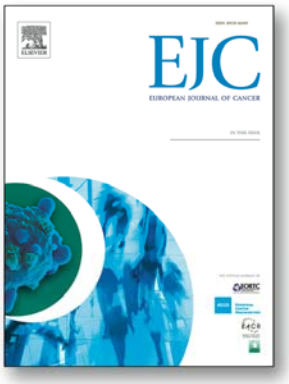

CT Regulation *continued.*

money that is invested in health research, only for vast quantities of it to be handed over to insurance companies," she said.

She described as "huge Improvements" the steps taken with the new Regulation as they would enable oncology researchers to do cross-border trials and make low intervention trials easier to conduct.

"At least the negotiations have forced EU countries to look at the problems around insuring clinical trials, and I hope more will consider introducing national indemnification systems after examining the models that already exist in Denmark and elsewhere," Wilmott said.

Overall, Blay sees the Regulation as a better law for the growing field of genomic- based oncology treatment. "We are in a world where genomics is completely changing the landscape for cancer and we have more and more molecular subgroups of disease being identified, which need specific treatment. "

He said that this results in a fragmentation of common cancers such as lung cancer, which is now split into different entities.

> ***'The life of a patient in The Netherlands, Germany, France or the UK should be indemnified under the same scheme'***
>
> **Françoise Meunier**
> **EORTC**

"The models of rare cancers, because of these molecular refinements, may become the rule and not the exception in the coming years. I think therefore rare tumours are good models for the future of oncology and the Clinical Trial Regulation will help progress in this direction," Blay concluded.

Jim McGuigan

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