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EDITORIAL

Data protection and research in the European Union: a major step forward, with a step back

After a lengthy process that began in 2012, the General Data Protection Regulation 2016/679 (GDPR) of the European Union (EU) finally came into force on 25 May 2018.[1] The past 8 years have seen numerous discussions surrounding the GDPR. Although health research is not one of its major focus areas, the GDPR has become a matter of great concern for the research community. After years of intense advocacy, supported by the entire European oncology community, the European Society for Medical Oncology (ESMO) and other co-signing parties found the final text of the GDPR to be a positive improvement over its originally approved version in 2014 by the European Parliament.[2] ESMO welcomed the text's recognition of the principle of 'one-time consent' for retrospective research and biobanking and the principle of 'no consent' for population-based registries, two concepts which were heavily advocated for by the oncology community over the years. However, the challenge of interpreting and implementing GDPR across all EU countries persists. In pursuing this goal, an EU body, the European Data Protection Board (EDPB) (which replaced the so called Article 29 Working Party) adopted guidelines, with some interpretations relating to scientific research, which are of major concern to the oncology community.[3] Certainly, many barriers remain in securing the future of research in the EU under a consistent and well-regulated framework.

ESMO immediately recognised the potential impact that the GDPR could have on research, which led to a 6-year-long advocacy action plan to protect the research community from potential unintended consequences of the Regulation. This action towards policymakers, supported by the entire European oncology community, advocated the idea that while fully protecting the privacy of patient data, the GDPR should not jeopardise clinical, translational and epidemiological research in the EU. This case was summarised in a position paper published in the *Annals of Oncology* in 2014.[4]

Undoubtedly, the GDPR is a crucial piece of legislation that will greatly impact the European research community, including oncology research. First, being a regulation, it directly became a part of Member States' laws, with no transposition. Second, the breadth of GDPR's impact on oncology research ranges from the usage of health data for retrospective clinical research and biobanking to population-based registries, starting with cancer registries.

Observational retrospective clinical research is the simplest form of research in medicine. It allows clinicians to look back at their previous patient cases and learn from them. This may translate into retrospective case series analyses or case reports, which in turn may directly constitute new knowledge or generate hypotheses to be tested through prospective clinical trials. Retrospective case series can also serve as external controls for uncontrolled prospective clinical studies. In addition to observational clinical research, retrospective research can be done on biological samples, that is, tumours or other tissues, which may be viewed as packages of personal data. The combination of clinical data and biological samples gives rise to 'biobanking', which is becoming an essential component of 'precision medicine'. In fact, having the ability to look back at clinically annotated biological samples is crucial for clinical and translational research.

Two issues regarding the ethics and legality of storing and using such data for research purposes need to be addressed. First, data and tissues should be stored under the safest conditions, so that a patient's privacy is protected by the highest standards possible. This strict protection of privacy should apply to all personal data that are stored, such as patient records kept in a hospital or surgically excised tumour samples hosted in the archives of a pathology department. Strict protection should be in place, independent of the planned use of data and tissues, whether for research or not. Evidently, any retrospective research, whether on health data or tissues, should undergo the scrutiny of institutional review boards, ethics committees, etc., so that patients' rights are protected with regard to what specifically takes place for research purposes.

Second, the patient also has the right, in principle, to be informed about the future use of his/her data and tissue samples for research purposes, that is, for nonclinical reasons. Informed patient consent is a crucial element of medical ethics. Thus, the patient should retain the right to consent or not, concerning the use of his/her data and biological samples for research purposes. If consent has been given, this should be withdrawable at any time (of course, before the use of data or tissues for a research project). However, in the context of the GDPR, the discussion around withdrawable one-time consent has focused on whether it should be 'specific', that is, to which extent should the specificity of the research carried out at any given time be detailed. In most cases, when data and tissue are stored, it is difficult to foresee any specific aim of future research. For example, the nature of agents that will be

discovered in the future cannot be foreseen at the time tissues are collected, say, when a tumour is surgically excised (and stored, for clinical purposes, in the hospital pathology department, or, deliberately for research purposes, in a biorepository).

Likewise, one cannot foresee whether and why patients' health data, automatically stored in the hospital's patient records (e.g. an electronic patient record), may become of interest to future retrospective research. Thus, if, say, a few patients' clinical data (that were collected and stored under strict safeguards) are used by a researcher, after several years, to retrospectively see whether they responded to a given medicine, would patients have to be 'reconsented'? Or if a sample of a patient's tumour tissue is assessed after many years for the expression of a molecular target hit by a new anticancer agent, would this mean that the researcher would need to seek the 'reconsent' of the patient? For reasons that are obvious to any clinician, reconsenting patients is often impossible, or at the very least highly burdensome, in addition to being unreasonably intrusive into a patient's life, given that they would be contacted after long intervals of time regarding a past disease. In practice, this may prevent physicians from using information that would otherwise be very easy to collect and would prove extremely useful for research. In reality, this would prevent patients from giving their initial consent to 'donate' data and/or tissues for research. In other words, the patient would have the right to dissent, but paradoxically would not have the right to consent in the first place. While it goes without saying that any consent should be withdrawable at any time (i.e. before the use of data or tissues), the lack of a withdrawable option to donate their data for further research would be illiberal towards patients and would violate certain human rights, such as the right to improving knowledge for the benefit of health. Ultimately, this is about the right to health.

Population-based disease registries provide an incredible array of data about how diseases behave, how quality of care affects their outcomes and how the data correlates with risk factors, among others. In oncology, the data collected through the registries are crucial to understand trends in cancer occurrence, to correlate survival with changes in health systems, to assess the outcome of newly implemented treatments, to plan new actions in health policy and to establish cancer plans and measure their effectiveness. Specifically, population-based cancer registries provide extremely useful information about incidence, prevalence and survival of cancer, and improve the understanding of evolving scenarios of cancer worldwide. These registries currently try to widen the scope of their data beyond basic information such as pathologic diagnosis and date of death.

It is trivial to note that for public health researchers to predict trends of disease, survival and any estimation of the future needs of a population, population-based disease registries need to collect the data of the entire population. Even a single patient dissenting would mean that data would be flawed and would not represent the entire population anymore. Thus, it is vital that population-based disease registries can work under 'no-consent' policies, as they serve a high public health interest and are subject to strict operational rules. While it is possible to define their setting and running procedures and responsibilities by means of the law, some kind of no-consent principle should be in place for them to survive.

The lengthy process of negotiations, amendments and compromises around the GDPR resulted in a text which considered the needs of the research community and alleviated our concerns. The final version of the GDPR reflects two main points concerning data being used for (i) retrospective, clinical and translational research, and (ii) epidemiological research. The points are explained via recitals, that is, those statements recalling the assumptions upon which articles are based. In other words, the articles of the GDPR should be interpreted through the accompanying recitals, two of them being relevant to the issues of research.

- GDPR Recital 33 acknowledges that 'it is often not possible to fully identify the purpose of personal data processing for scientific research purposes at the time of data collection'.[1] In other words, this recognises that the subject of future research may be unknown at the time a patient gives his/her consent on the use of clinical data for scientific purposes. The Recital further states that patients '(…) should be allowed to give their consent to certain areas of scientific research when in keeping with recognised ethical standards for scientific research'. Depending on the patient's wishes, the consent can also be given 'only to certain areas of research or parts of research projects', and of course, any consent can be withdrawn.

Importantly, another recently approved EU Regulation, the Clinical Trials Regulation EU No 536/2014 (CTR), will come into operation when the 'full functionality' of the Clinical Trials Information System is achieved. The new Regulation specifically incorporates the notion of a 'one-time consent'.[5] Recital 29 of the CTR acknowledges that:

'it is appropriate that universities and other research institutions, under certain circumstances that are in accordance with the applicable law on data protection, be able to collect data from clinical trials to be used for future scientific research, for example for medical, natural or social sciences research purposes. In order to collect data for such purposes it is necessary that the subject gives consent to use his or her data outside the protocol of the clinical trial and has the right to withdraw that consent at any time'.

Furthermore, in the CTR, Article 28 reinforces the aforementioned Recital (as the two are to be read in conjunction with each other) and allows the patient to 'give (…) his or her informed consent to participate in the clinical trial to consent to the use of his or her data outside the protocol of the clinical trial exclusively for scientific purposes'.[3] In other words, the notion of a 'one-time consent'

is fully acknowledged by this EU Regulation with regard to clinical trials, this being the scope of the Regulation. In this case, the 'one-time consent' is given to use data retrospectively beyond the end and scope of a clinical trial. All this must take place 'without prejudice' to the data protection provisions, that is, should comply with the framework of the GDPR.

- With respect to epidemiological research, GDPR Recital 157 acknowledges that 'by coupling information from registries, researchers can obtain new knowledge of great value with regard to widespread medical conditions such as cardiovascular disease, cancer, and depression'.[1] The Recital reiterates that 'research results obtained through registries provide solid, high-quality knowledge which can provide the basis for the formulation and implementation of knowledge-based policy, improve the quality of life for a number of people and improve the efficiency of social services'. Therefore, 'in order to facilitate scientific research, personal data can be processed for scientific research purposes, subject to appropriate conditions and safeguards set out in Union or Member State law'. Simply put, registries should be allowed to process data even without patient consent, provided that privacy-protecting safeguards are complied with. Lastly, GDPR Recital 52 reinforces the aforementioned by stating that:

'derogating from the prohibition on processing special categories of personal data should also be allowed when provided for in Union or Member State law and subject to suitable safeguards, so as to protect personal data and other fundamental rights, where it is in the public interest to do so, in particular processing personal data in the field of employment law, social protection law including pensions and for health security, monitoring and alert purposes, the prevention or control of communicable diseases and other serious threats to health. Such a derogation may be made for health purposes, including public health and the management of health-care services'.[1]

The GDPR came into force on 25 May 2018. Significantly, GDPR is a 'regulation' and not a 'directive', as compared with its predecessor on data protection (the 1995 Data Protection Directive, 1995/46/EC). A regulation differs from a directive because it is immediately binding on all EU countries, with no need for further national provisions by national ruling bodies (i.e. parliaments or governments). This is important because, in principle, it should ensure that what has been agreed upon between EU institutions and Member States is implemented consistently across the EU. In fact, with respect to data protection, this was the aim: creating a regulation instead of another directive. However, it is important to note that, in certain cases, the wording of a regulation can still be interpreted on the lines of a directive, that is, on a Member State-by-Member State basis.

Specifically, in the case of the GDPR, its provisions are to be implemented across the EU countries through national 'authorities'. Throughout the last 6 years, on behalf of the oncology community, ESMO continuously stressed that it is crucial to have a harmonious implementation of the GDPR, specifically in the interest of research in the EU. The previous Directive 1995/46/EC resulted in a fragmented approach of data protection provisions across the EU, allowing some countries to foster research and others to create unattractive research environments. An uneven implementation of any EU rule would be an obstacle for collaborative research across EU countries, which would face additional difficulties due to discrepancies in national policy and regulations.

As of 25 May 2018, the implementation date of the GDPR, the EU body 'Article 29 Working Party' was replaced by the European Data Protection Board (EDPB). The EDPB is the independent EU body which oversees the application of data protection rules, ensuring they are consistent across the EU and safeguarding cooperation between the EU's data protection authorities. Their role includes delivering guidelines to ensure the core concepts of the GDPR are equally interpreted, and they oversee data processing disputes between EU Member States. In theory, this body should guarantee that such cases will be dealt with in a uniform manner, thus ensuring the GDPR is effectively upheld in each case.

The guidelines on consent delivered by the Article 29 Working Party were last revised and adopted on 10 April 2018, and the EDPB published its version on 4 May 2020. The guidelines intend to clarify any ambiguous definitions set out within the GDPR articles. This includes the concept of specifying the future purpose of data use, mentioned earlier in GDPR Recital 33. The EDPB guidelines acknowledge that there is flexibility surrounding the degree of specification of consent and advise that 'applying the flexible approach of Recital 33 will be subject to a stricter interpretation and requires a high degree of scrutiny' to special categories of data.[3] Despite the intent to clarify how to deal with the uncertainty within the Recital, the guidelines therefore still leave room for discrepancies over what constitutes 'a high degree of scrutiny', meaning the guidance still allows for a discrepant interpretation of the text.

Two years into the GDPR's implementation and corresponding guidelines, ESMO has witnessed concrete examples of inconsistencies between several Member States where the 'interpretations' of the Regulation are applied on the ground in varying and concerning ways from country to country. This is a result of major discrepancies at national levels, where national guidelines being provided are either differing, or, in some instances, do not exist at all. While the guidance provided by the EDPB is indeed crucial to the harmonious interpretation of the GDPR across the EU, ESMO asserts that the ambiguous guidance provided, specifically on aspects related to consent and health research, is resulting in a fragmented implementation of the GDPR, giving rise to the same issues as the previous Directive. It is therefore important to work together with the EDPB, the EU Member States and other supervisory authorities to

harmonise the application of the GDPR. This is especially vital when it comes to sharing data for research purposes, within but also outside the EU (including the European Economic Area and the United Kingdom). More research should be done on how to best share high-quality health data for health research in a secure manner, for instance, by promoting research into new technologies.

As this is a serious cause for concern for future research, ESMO urges the EU Member States to take the following into consideration, while implementing the GDPR:

- GDPR Recital 33 should be acknowledged as a means to guarantee, in all EU Member States, that patients have the right to provide, if willing, a withdrawable 'one-time consent' to using their data and/or biological samples for future retrospective research, under the scrutiny of appropriate reviewing bodies (institutional review boards and/or ethics committees);
- GDPR Recital 157 should be acknowledged as a means to guarantee that in all EU Member States, population-based disease registries, including cancer registries, are allowed to operate with a 'no-consent' policy under the supervision of relevant public health bodies;
- Recital 29 and Article 28 (2) of the CTR should be implemented across the EU 27 to give patients enrolled in a clinical trial the right to consent that their data to be used retrospectively beyond the end and scope of the trial for future research.

The new Data Protection framework is being implemented across the EU Member States and has significant potential to safeguard data rights in the realm of health research. The European Parliament, Commission and Council have worked tirelessly to create this important framework, which aims to create a positive and protected environment for data use and the user. The GDPR was welcomed by the entire oncology community, specifically concerning the aforementioned principles explained in Recitals 33 and 157, consistent with Recital 29 and Article 28 (2) of the CTR. We now have an opportunity to ensure that these principles are in fact harmonised across all EU Member States, in order to allow health research to continue in a secure manner, and rely on Member States to uphold the essential concepts outlined in the GDPR, using the EDPB guidelines as guidance to try to remain consistent with one and the other. Patients should be free to consent, if willing, to donate their data for health-research purposes with strict safeguards in place. This is crucial for the future of health research. Denying this would mean denying a patient's basic civil right.

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Available online 21 October 2020
https://doi.org/10.1016/j.annonc.2020.10.472

ACKNOWLEDGEMENTS

The authors wish to acknowledge the support and contributions of the ESMO Executive Board, as well as the societies endorsing this manuscript, listed below.

ENDORSEMENTS

Endorsements

European Organisation for Research and Treatment of Cancer

European Society of Surgical Oncology

European Society for Paediatric Oncology

European SocieTy for Radiotherapy and Oncology

European Cancer Patient Coalition

Association of European Cancer Leagues (ECL)

FUNDING

None declared.

DISCLOSURE

PGC reports: In the last 3 years, I have had honoraria for speaker, consultancy or advisory role from Bayer, Deciphera, Eisai, Eli Lilly, Nektar Therapeutics, Pfizer. At my institution, my Unit received funds from Advenchen Laboratories, Amgen Dompé, AROG Pharmaceuticals, Bayer, Blueprint Medicines, Daiichi Sankyo, Deciphera, Eisai, Eli Lilly, Epizyme Inc, Glaxo, Karyopharm Pharmaceuticals, Novartis, Pfizer, PharmaMar. MV reports being an employee of the European Society for Medical Oncology.

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