In preparation for the IPMPC-MedTech Europe Workshop on Data Protection in Health Research we are issuing a series of Briefing Papers. This is the fourth in the series. Please visit *https://www.ipmpc.org/dpa-workshop* to access the other papers.

IPMPC
International Pharmaceutical & Medical Device Privacy Consortium

IPMPC BRIEFING PAPER #4

REAL-WORLD DATA AND HEALTH RESEARCH

Issue: *Real-world data sources such as patient registries, electronic health records, and health care claims databases provide useful information on the quality, safety, and effectiveness of medicines and medical devices. When personal data that was collected for one purpose is further processed for another purpose, the issues of compatibility of processing, the lawful basis for processing, transparency, and a data subject's right to object are particularly acute. This paper explores these issues.*

BACKGROUND

Real-world data refers to data collected outside of randomized controlled trials. In a randomized controlled trial, participants are randomly allocated to either a group receiving the drug, device, or other treatment under investigation or a group receiving standard treatment or a placebo treatment as the control. While randomized controlled trials are generally considered the 'gold standard' for demonstrating safety and efficacy, there are inherent limitations. For example, some experimental questions do not allow for random allocation of treatments due to ethical concerns. Moreover, the population as a whole tends to be more heterogeneous than the population of individuals who participate in clinical trials. The behavior of patients and clinicians is also more variable in the real world than in controlled, experimental settings. As a result, an 'efficacy-effectiveness gap' can occur – i.e., a gap between the 'efficacy' of a test article as measured in randomized controlled trial settings and the 'effectiveness' as measured in real-world, clinical practice.

Collection and analysis of real-world data serves a number of important research purposes. First, it enables a more robust assessment of the safety and effectiveness of a health care product in clinical practice. This includes the identification of populations for whom the product is more, or less, safe/effective. This information, in turn, informs clinical decision-making and, in some cases, can even lead to a change in product labelling. Second, it enables the evaluation of the relative effectiveness of a new product as compared with other, existing products in clinical practice. This also informs clinical decision-making and can influence reimbursement decisions.

EXISTING SOURCES OF REAL-WORLD DATA

Real-world data can be obtained by conducting new studies or by utilizing existing data sources. If the researcher desires to generate new data, experimental studies with methodologies that deviate from typical randomized controlled trials can be designed, or observational studies without any experimental interventions can be conducted. In many cases, however, existing data sources may meet a researcher's needs. These data sources include:

Patient Registries

A patient registry collects observational information over time on a defined patient population, such as patients who share a particular disease or condition, or patients who have received a particular treatment. Some patient registries are funded by government agencies while others are supported by patient advocacy groups, research institutions, or other non-governmental organizations. A manufacturer may establish a product-specific registry to monitor the long-term safety of one of its products, for example. In some cases, the clinical information stored in a registry is supplemented by biological samples stored in a biobank.

Electronic Health Records

Electronic health records (EHRs) refer to the medical records maintained in electronic databases by health care providers. These records may include data collected during clinical encounters, as well as results of laboratory tests and medical imaging. Across the EU, many countries have invested in the development of national infrastructures to support EHRs, and a key challenge now is to promote interoperability so that these records are accessible throughout the EU. The European Commission's eHealth Digital Service Infrastructure project aims to enable, in the short-term, the exchange of e-prescriptions and patient summary information, so that prescriptions and emergency care can be provided when patients are traveling. In the longer term, the Commission's strategy calls for the development and adoption of a European electronic health record exchange format.

Health Claims Databases

Health care claims databases contain information submitted to payers when a health care provider submits a claim for reimbursement. They may include information on services performed and treatments dispensed. Because these types of databases are intended for payment and other administrative purposes, the records may have limited clinical information.

LAWFUL BASIS FOR PROCESSING

The GDPR recognizes the importance of being able to conduct health research using real-world data. For example, Recital 157 states:

> *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. On the basis of registries, research results can be enhanced, as they draw on a larger population. . . . 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. 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.*

The GDPR allows for explicit consent to be obtained from data subjects to the use of their data for future scientific research purposes. Recital 33 acknowledges that '[i]t is often not possible to fully identify the purpose of personal data processing for scientific research purposes at the time of data collection.' Therefore, 'data subjects should be allowed to give their consent to certain areas of scientific research when in keeping with recognised ethical standards for scientific research. Data subjects should have the opportunity to give their consent only to certain areas of research or parts of research projects to the extent allowed by the intended purpose.' Reliance on consent as a legal basis for processing of personal data may be most practical in the real-world data context in those situations where future use of the data for health research purposes is envisioned at the time of data collection.

For example, some patient registries are established for the express purpose of creating a repository of research information. In those circumstances, express consent to the future research may be able to be obtained at the time of data collection.

In other circumstances, however, reliance on consent as a legal basis for processing may be less practical. For example, EHRs are created for health care delivery purposes and their use for research purposes pursuant to consent would typically require contacting the patients. While some EHR systems have been created with this in mind, in most cases this would require significant effort and resources. The GDPR provides alternative options for researchers to consider.

Processing for Scientific Research Purposes

Pursuant to GDPR Articles 5.1(b), 6.1(f), 9.2(j), and 89.1, personal data can be processed for scientific research purposes where the processing meets certain criteria. Recital 159 elaborates on what constitutes 'scientific research' for these purposes: 'For the purposes of this Regulation, the processing of personal data for scientific research purposes should be interpreted in a broad manner including for example technological development and demonstration, fundamental research, applied research and privately funded research.' While no formal definition of 'research' is found in the GDPR, other European projects have sought to tackle the question of 'what is research'? For example, the *European Textbook on Ethics in Research* (commissioned by the European Commission in 2010) proposes the following working definition: 'Research aims to generate (new) information, knowledge, understanding, or some other relevant cognitive good, and does so by means of a systematic investigation.' The qualifier 'scientific,' as used in the GDPR, may be aimed at distinguishing research concerning the structure and behaviour of the physical and natural world – including biomedical research – from other types of research (for example, from marketing research).[1] In any event, as is made clear in Recital 159, 'scientific research' can be publicly and/or privately funded.

Processing for scientific research purposes must be pursuant to appropriate technical and organizational safeguards. Article 89.1 specifies that these safeguards may include the pseudonymisation of the data. Further, the data should be fully anonymised if anonymised data would fulfil the researchers' purposes.

When relying on the derogation in Article 9.2(j) to process sensitive personal data for scientific research purposes, the processing must be 'on the basis of [European] Union or Member State law'. The EU or Member State law in question 'must be proportionate to the aim pursued, respect the essence of the right to data protection and provide for suitable and specific measures to safeguard the fundamental rights and the interests of the data subject.'[2] GDPR Recital 41 serves to clarify what can qualify as 'based on EU or Member State law'. Recital 41 indicates that references in the GDPR to a legal basis or a legislative measure do not necessarily require a legislative act adopted by a parliament but rather simply require a legal measure 'clear and precise' and foreseeable in its application by persons subject to it.

Processing for Reasons of Public Interest in the Area of Public Health

GDPR Article 9.2(i) provides another derogation to the prohibition on processing of sensitive personal data that is relevant in the context of medicinal products and medical devices. This derogation applies where 'processing is necessary for reasons of public interest in the area of public health, such as . . . ensuring high standards of quality

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[1] In its *Guidelines on Consent Under Regulation 2016/679*, the Article 29 Working Party states that it interprets 'scientific research' in the context of the GDPR as meaning 'a research project set up in accordance with relevant sector-related methodological and ethical standards, in conformity with good practice'.

[2] *See* Art. 9.2(j). *See also* Recital 52.

and safety of health care and of medicinal products or medical devices, on the basis of Union or Member State law which provides for suitable and specific measures to safeguard the rights and freedoms of the data subject, in particular professional secrecy.'

There appears to be overlap in the application of GDPR Article 9.2(j) (the scientific research derogation) and Article 9.2(i) (the public health interest derogation) to research related to the quality and safety of marketed medicines and medical devices. One open question is whether the slight difference in the language concerning the EU or member state law on which the processing must be based has any substantive impact (*i.e.*, while both derogations state that this law must 'provide for suitable and specific measures to safeguard the fundamental rights and the interests of the data subject', the scientific research derogation adds that this law must 'be proportionate to the aim pursued [and] respect the essence of the right to data protection').

TRANSPARENCY

Pursuant to GDPR Articles 13 and 14, controllers must provide data subjects with certain information concerning the processing of personal data about them. Where the data is collected from someone other than the data subject, the information must be provided 'within a reasonable period after obtaining the personal data'.[3] However, an exception to the requirement to provide this information is available where 'the provision of such information proves impossible or would involve a disproportionate effort, in particular for processing for . . . scientific . . . research purposes . . . , subject to the conditions and safeguards referred to in Article 89(1) or in so far as the obligation [to provide the information] is likely to render impossible or seriously impair the achievement of the objectives of that processing.'[4] The exception goes on to require that '[i]n such cases the controller shall take appropriate measures to protect the data subject's rights and freedoms and legitimate interests, including making the information publicly available.' Recital 62 states that in evaluating whether providing notice involves disproportionate efforts, 'the number of data subjects, the age of the data and any appropriate safeguards adopted should be taken into consideration.'

The Article 29 Working Party has stated in its *Guidelines on Transparency Under Regulation 2016/679* that where a controller seeks to rely on the above exception, it must undertake a balancing exercise to assess the effort involved to provide the information against the effects on the data subject if the information is not provided.[5] The Working Party further states that where the exception applies, the information must be made publicly available and other appropriate measures may include undertaking a data protection impact assessment, applying pseudonymisation techniques to the data, minimising the data collected and storage period, and implementing security safeguards.

RIGHT TO WITHDRAW CONSENT OR OBJECT TO THE PROCESSING

As noted, if consent is relied upon as a legal basis for the processing of personal data, the data subject has the right to withdraw consent at any time. The Article 29 Working Party has opined in its *Guidelines on Consent Under*

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[3] Art. 14.3(a).

[4] Art. 14.5(b).

[5] Article 29 Working Party, *Guidelines on Transparency Under Regulation 2016/679* (11 April 2018) at § 64.

Regulation 2016/679 that where consent is relied upon as a legal basis for processing, it would not be fair to allow the controller to switch legal bases upon withdrawal of consent.[6]

The right to object to processing applies whenever the legal basis for processing is 'the performance of a task carried out in the public interest' (GDPR Art. 6.1(e)) or the 'legitimate interests' of the controller (Art. 6.1(f)).[7] The data subject's objection must be based 'on grounds relating to his or her particular situation'. The controller is obliged to cease processing the data unless it can demonstrate 'compelling legitimate grounds' for the processing which override the data subject's rights and interests. The Article 29 Working Party has noted that the GDPR does not explain what grounds would be considered compelling, but it is implied that this is a higher threshold than the legitimate interests balancing test under Art. 6.1(f).[8]

In addition, the data subject has a right to object to processing for scientific research purposes pursuant to Article 89.1.[9] Again, the data subject's objection must be based 'on grounds relating to his or her particular situation', but in this circumstance the controller is obliged to cease processing the data 'unless the processing is necessary for the performance of a task carried out for reasons of public interest'.

CONCLUSION

The GDPR provides mechanisms to process real-world data for health research purposes. However, the need for such processing to be based on EU or member state law in order to take advantage of these mechanisms creates considerable uncertainty. Moreover, careful consideration needs to be given to how best to comply with the principle of transparency. In any event, data subjects can generally object to this processing, although this right might be limited in situations in which the need to analyse the data is compelling (e.g., monitoring and reporting on product safety).

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[6] Article 29 Working Party, *Guidelines on Consent Under Regulation 2016/679* (10 April 2018) at § 6.

[7] Art. 21.1.

[8] Article 29 Working Party, *Guidelines on Automated Individual Decision-making and Profiling for the Purposes of Regulation 2016/679* (6 February 2018), at 18-19.

[9] Art. 21.6.