

# Addressing choice of law challenges in multi-state precision medicine research: experts' assessment of key factors

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## ABSTRACT

Precision medicine research implicates numerous state laws that may affect participants' rights and protections and are not preempted by federal law. The choice of which state's laws apply, and under what circumstances, can have significant impact on research design and oversight. But neither of the traditional approaches to choice of law issues—contractual agreement or determination by a court after a dispute arises—fit the research context well. We hosted a series of workshops with choice of law experts and research law and ethics experts to identify factors that are most crucial to account for in a future choice of law precision medicine research framework. Our workshops focused on precision medicine 'places' and choice of law factors; there was consensus that 'place where the harm occurred' was relevant and best represented by where the participant resides and/or where the research/institution is located. Our experts identified factors that need to be accounted for in a future choice of law framework. They also identified potential approaches, including a federal law or model state law as ways of achieving more uniformity of protections and a comprehensive database of laws, which merit further consideration to provide IRBs and researchers the guidance they require.

**KEYWORDS:** precision medicine research, choice of law, human subjects protections, law, research ethics

Precision medicine research implicates numerous state laws that govern an array of topics—human subjects research, genetic testing, and both general and genetic privacy and discrimination to name a few—that are not preempted by federal law.<sup>1</sup> Thus, the choice of which state’s laws apply, and under what circumstances, can have significant impact on research design and substantive legal protections for participants. Outside the research context, parties entering into contracts or other agreements may specify in advance which state’s laws will apply.<sup>2</sup> When there is no such agreement and a dispute arises, judges determine which state’s laws apply according to existing choice of law frameworks.<sup>3</sup> However, in the context of research, the first option is not available because federal regulations governing human subjects protections (the ‘Common Rule’) prohibit ‘exculpatory clauses’ that waive legal rights in consent forms.<sup>4</sup> Moreover, uncertainty over whether and how different state’s laws might apply presents challenges in the design and oversight of multi-state precision medicine research and complicates determinations of institutional obligations and liability in the event a participant is harmed.

We first conducted qualitative interviews with key informants to learn about experiences with and perceptions of choice of law questions in the research context.<sup>5</sup> While experiences and perceptions varied among our informants, some readily identified choice of law as an issue they already confront, and a few characterized variation in participant rights and protections based on state law as ethically troubling. Yet there is little consensus or guidance on how to address these issues.<sup>6</sup> In this project, we hosted a series of workshops with choice of law experts and research law and ethics experts as a first step to understanding the factors that are relevant to choice of law questions in the precision medicine context. With the traditional choice of law tools unavailable, the workshops were designed to elicit creative thinking, unconstrained by existing choice of law or human subjects protections frameworks. We sought this expert feedback to identify the most relevant factors for choice of law questions in precision medicine research to inform future research that might ultimately lead to a way to address choice of law issues in precision medicine research.

## I. BACKGROUND ON PRECISION MEDICINE RESEARCH

Precision medicine has been defined as ‘an approach to disease treatment and prevention that seeks to maximize effectiveness by taking into account individual variability in genes, environment, and lifestyle . . . through more precise measurement of molecular,

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1 Leslie E. Wolf, et al., *The Web of Legal Protections for Participants in Genomic Research*, 29 HEALTH MATRIX 1 (2019); Leslie E. Wolf, et al., *Protecting Participants in Genomic Research: Understanding the ‘Web of Protections’ Afforded by Federal and State Law*, 48 J. LAW MED. ETHICS 126 (2020).

2 John F. Coyle, *The Canons of Construction for Choice-of-Law Clauses*, 92 WASH. L. REV. 631 (2017); Erin Ann O’Hara, *Opting Out of Regulation: A Public Choice Analysis of Contractual Choice of Law*, 53 VAND. L. REV. 1551 (2000).

3 PATRICK J. BORCHERS, *CONFLICTS IN A NUTSHELL* (West Academic Publishing, 2016); SYMEON C. SYMEONIDES, *THE AMERICAN CHOICE-OF-LAW REVISION: PAST, PRESENT AND FUTURE* (Koninklijke Brill NV, 2006).

4 45 C.F.R. 46.116 (2019).

5 Laura M. Beskow, et al., *Perspectives on choice of law challenges in multi-site precision medicine research*, J. LAW & BIOSCIENCES (accepted for publication, 2022).

6 *Id.*

environmental, and behavioral factors that contribute to health and disease'.<sup>7</sup> Research conducted to advance precision medicine requires massive amounts of data from hundreds of thousands of participants. For example, two federal projects, the All of Us Research Program and the Million Veteran Program, have each set a goal to recruit a million participants, compared to the hundreds or thousands commonly enrolled in traditional clinical research.<sup>8</sup> The scale of these projects—in terms of number and types of sites, participants, data collected, and questions addressed—coupled with evolving information risks create new challenges.

Data may be stored at one institution, analyzed at another, and the principal investigator located at yet another. Participants may be located anywhere. Moreover, participants may not have direct contact with researchers, as consent can be completed remotely, biospecimens can be collected at home, and a slew of data can be collected electronically on an ongoing basis. Accordingly, unlike a traditional clinical research study, there are numerous places where it could be said the research is being 'conducted'. In addition, the research data are collected for long-term study without a defined research question. Participants agree broadly to research use rather than specific studies, with an entity such as an institutional review board or data access committee making determinations about whether a particular project or researcher can access and use the data.<sup>9</sup> The longitudinal nature of precision medicine research requires data remain identifiable. While researchers using the data typically will not have access to identifiers, preserving confidentiality is difficult in an era of whole genome sequencing and a proliferation of data that can be combined from different sources.<sup>10</sup>

## II. SIGNIFICANCE OF THE CHOICE OF LAW ISSUE FOR PRECISION MEDICINE RESEARCH

In our previous research, the thought leaders we interviewed identified a variety of risks and harms presented by precision medicine research.<sup>11</sup> These included physical risks and harms that could arise from interventions undertaken based on individual research results. Individuals could suffer dignitary harms when their data are used for research

7 National Institutes of Health, *Report to the Advisory Committee to the Director, NIH, The Precision Medicine Initiative Cohort Program—Building a Research Foundation for 21st Century Medicine*. (2015). (accessed December 14, 2021).

8 Francis S. Collins & Harold Varmus, *A New Initiative on Precision Medicine*, 372 N. ENGL. J. MED. 793 (2015); U.S. Department of Veterans Affairs, *Office of Research & Development, Million Veteran Program (MVP)*, <https://www.research.va.gov/mvp/>.

9 Christine Grady, et al., *Broad Consent for Research With Biological Samples: Workshop Conclusions*, 15 AM. J. BIOETH. 34 (2015).

10 Eric E. Schadt, *The Changing Privacy Landscape in the Era of Big Data*, 8 MOL. SYST. BIOL. 612 (2012); Laura L. Rodriguez, et al., *Research Ethics. The Complexities of Genomic Identifiability*, 339 SCIENCE 275 (2013); Jennifer Kulynych & Henry T. Greely, *Clinical Genomics, Big Data, and Electronic Medical Records: Reconciling Patient Rights With Research When Privacy and Science Collide*, 4 J. LAW & BIOSCIENCES 94 (2017); Mark A. Rothstein, *Ethical Issues in Big Data Health Research: Currents in Contemporary Bioethics*, 43 J. LAW MED. & ETHICS 425 (2015); Mark A. Rothstein, *Some Lingering Concerns about the Precision Medicine Initiative: Currents in Contemporary Bioethics*, 44 J. LAW MED. & ETHICS 520 (2016).

11 Laura M. Beskow, et al., *Thought Leader Perspectives on Benefits and Harms in Precision Medicine Research*, 13 PLOS ONE e0207842 (2018); Laura M. Beskow, et al., *Thought Leader Perspectives on Risks in Precision Medicine Research*, in *BIG DATA, HEALTH LAW, AND BIOETHICS* (I. G. Cohen, et al. eds., 2018); Catherine M. Hammack, et al., *Thought Leader Perspectives on Participant Protections in Precision Medicine Research*, 47 J. LAW MED. & ETHICS 134 (2019).

they consider objectionable, and group harms could result from research findings that reflect negatively on specific populations. Economic or financial harms may occur, for example, through discrimination in employment and insurance. Psychological harms could arise from return of individual research results, unintended access to stored data, or the open-ended nature of the research. Legal harms may also arise should law enforcement or other government entities access and use research data, the Golden State Killer case serving as one commonly raised example.<sup>12</sup>

Researchers are most familiar with the federal laws that address participants' rights and protections, including the Common Rule, the HIPAA Privacy and Security Rules, Certificates of Confidentiality, and the Genetic Information Nondiscrimination Act (GINA).<sup>13</sup> However, these laws have well-known gaps.<sup>14</sup> Our previous research revealed numerous state laws that fill some of these federal gaps and provide substantive rights and protections that federal law does not.<sup>15</sup> For instance, State A may require specific consent to use a participant's genetic information for secondary research, whereas federal rules allow for broad consent. State B may allow participants to recover statutory minimum damages, as well as attorneys' fees and costs in the event their genetic information is breached, whereas federal law does not even provide for a right to sue directly for breach. State C may go beyond GINA, which applies to health insurance and employment, to prohibit disability or life insurers from discriminating based on an individual's genetic information.<sup>16</sup> State D may require participants have an opportunity to receive results of genomic testing. As a result, participants' rights and protections in the same study may vary depending on which state applies, which in turn may depend on which of the many 'places' associated with precision medicine applies. These differences could also impact research design by, for example, altering whether and how consent is obtained for secondary research to accommodate State A's requirements, which may limit the data available for such research, or avoiding recruitment in certain states (e.g., States A and D), with adverse effects on the representativeness of the sample.

The variation in state law is considerable and idiosyncratic; there is not one state or group of states that consistently affords more protections than others. Some state law variations, such as age of majority for purposes of consent are relatively easily addressed and present few ethical concerns. But other variation results in differences in substantive rights and protections, like State A's giving participants control over each research use of their biospecimens, State B's remedies and State C's expansions of GINA's protections, which cannot be reconciled. Researchers simply do not have the power to extend those substantive rights and protections to states that have not adopted them. These examples illustrate the challenges in the design and oversight of

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12 Thomas Fuller, *How a Genealogy Site Led to the Front Door of the Golden State Killer Suspect*, N.Y. TIMES, April 26, 2018; Thomas Fuller, *Genealogy Websites Were Key to Big Break in Golden State Killer Case* NEW YORK TIMES, April 26, 2018.

13 45 C.F.R. 46 (2019); HIPAA Privacy Rule, 45 C.F.R. 160, 162, and 164; 42 U.S.C. § 241(d) (2018); Genetic Information Nondiscrimination Act of 2008, Pub.L. 110-233, 122 Stat. 881 (2008).

14 Hammack, et al. (2019) *supra* note 11.

15 Wolf, et al., HEALTH MATRIX, (2019) *supra* note 1; Wolf, et al., J. LAW MED. & ETHICS, (2020) *supra* note 1.

16 *Id.*

multi-state precision medicine research, including the development of unified consent language that informs participants of their rights and protections.

### III. BACKGROUND ON CHOICE OF LAW

Neither of the traditional approaches to choice of law issues—contractual agreement or determination by a court after a dispute arises—fit the research context well. In addition to the Common Rule’s prohibition on exculpatory clauses, researchers have continuing obligations to participants to provide the information necessary for them to decide whether to enroll and continue in research.<sup>17</sup> Although they are required to disclose research risks, consent forms do not typically include details concerning subsequent harms or specific rights and remedies—let alone how these vary by state.<sup>18</sup> Were researchers to explain these realities, it could affect how prospective participants perceive the risks and their willingness to participate. Moreover, even if the Common Rule were altered to allow a choice of law provision in a consent form, it is not clear that it would be enforceable because research consent forms are generally not considered binding contracts.<sup>19</sup>

Outside of the research context, multiple frameworks have been proposed to resolve choice of law questions when there is no contractual agreement.<sup>20</sup> The simplest is *lex loci delicti*, which looks to the place where the wrong occurred; for example, the state where a car accident occurred, even if the parties to the accident are non-residents. A similar framework, *lex loci contractus*, applies to where the contract was formed or intended to be formed. Other frameworks look to government interests, the state with the ‘most significant relationship,’ or to the ‘better law’. Each of these frameworks includes multiple factors, although no framework specifies how the factors should be weighted or considered together. Furthermore, it is unclear whether these or other factors are relevant to precision medicine research, which involves multiple locations, stakeholders, relationships, interests, and potential harms.

In this project, we sought initial input from experts to interrogate the factors that are most relevant to choice of law questions in the precision medicine context. The insights gleaned from these experts can inform future research that may ultimately lead to a new framework or approach that helps researchers and IRBs address choice of law challenges in the design and conduct of multi-state precision medicine research. This project adds to what we learned from our interviews with key informants about their experiences with choice of law questions.<sup>21</sup> Those interviews revealed different responses to the variation in state law they face in their reviews. Some did not view it as a problem because they apply their own state’s laws. Others saw the variation primarily as a logistical problem of identifying and interpreting the relevant laws to apply. Finally, others characterized the variation as an ethical problem because it results in differential rights and protections for participants in the same study, whereas others accepted the

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17 Graeme Laurie & Emily Postan, *Rhetoric or Reality: What is the Legal Status of the Consent Form in Health-Related Research?*, 21 MED. LAW. REV. 371 (2013).

18 Beskow et al., *supra* note 5.

19 Natalie Ram, *Assigning Rights and Protecting Interests: Constructing Ethical and Efficient Legal Rights in Human Tissue Research*, 23 HARV. J. LAW & TECH. 120 (2009).

20 SYMEONIDES. 2006 *supra* note 3; BORCHERS. 2016 *supra* note 3.

21 Beskow, et al., *supra* note 5.

variation as a part of daily life, which, to the extent the variation reflects the unique needs of populations, could be beneficial.

## IV. THE WORKSHOPS

### IV.A. Experts

For our workshops, we identified and invited prominent scholars and leaders in choice of law and experts in research law and ethics to participate. For both groups, we looked to their scholarly publications (including articles and casebooks) and their policy contributions (eg, service to the Secretary's Advisory Committee for Human Research Protections and to the American Law Institute RESTATEMENT ON CONFLICTS OF LAW). We limited the size of the workshop to 12 experts, evenly divided between choice of law and research law and ethics, to promote dynamic discussion. Because of the pandemic, we changed from a 1.5-day in-person workshop to three online workshops over three consecutive weeks. Ultimately, 11 experts (5 choice of law and 6 research law and ethics experts) participated, with some intermittent absences due to scheduling conflicts. All of the experts have law degrees, and five also have degrees in other disciplines. The majority of our experts (9/11 overall and 5/5 of our choice of law experts) are academics; seven have their primary appointment in a law school, and two have their primary appointment in a medical school. The remaining experts include a lawyer who represents academic institutions and another who has a leadership position at an independent IRB.

Given their disparate areas of expertise, we sent background materials to our experts before the first workshop. In addition to information about our research team and the experts participating in the workshop, we provided a brief introduction to precision medicine, precision medicine research, and a summary of our own research on the risk and protections in precision medicine research.

### IV.B. Workshop design and conduct

#### *Overview*

During each of the three workshops, we engaged our experts in activities designed to identify the factors that were most relevant to account for in a future choice of law precision medicine research framework and to begin to explore the relationships between them. Day 1 lasted three hours and focused on the various precision medicine research places to identify which, if any, were relevant to determining which law should apply. Day 2 also lasted three hours and focused on choice of law factors in the context of different research scenarios.

Before the Day 1 and Day 2 Workshops, we sent our experts the worksheets that would guide their deliberations (see [Appendix 1](#)). At the start of these workshops, after we provided an orientation to the material and the tasks for the day (described in more detail below), we asked our experts to fill out the worksheet associated with each task individually to prime the discussion for the next step. We then sent the experts to one of three virtual breakout rooms for small group discussion; each small group included choice of law and research law and ethics experts. There were also two research team members in each breakout room. Because we did not want our own views to influence deliberations, the research team members acted as observers and timekeepers, rather

than as facilitators. We asked each group to discuss and complete the worksheet for the task again within their group. We then reconvened the small groups in the main room to report their work. We altered the order in which small groups reported in the large group to ensure that no group's thinking dominated the results. This process was repeated for each task of the day.

On Day 3, we convened our experts for one hour to share our preliminary analysis of the information we received during Days 1 and 2 to ensure that we accurately reflected their input and to elicit any further feedback. We recorded all three workshop sessions.

### *Day 1*

Our first workshop focused on precision medicine places. Based on our knowledge of precision medicine research and choice of law frameworks, we identified the following places as potentially relevant to deciding which state's laws should apply:

- Where the participant currently resides
- Where the participant consented to study participation (eg, signed the consent form)
- Where the principal investigator/research entity of the overall study is located<sup>22</sup>
- Where the participant's biospecimens and/or data are stored
- Where the participant's biospecimens and/or data are analyzed

Furthermore, we anticipated that the relevance of each place might differ depending on whether the choice of law context was (i) upfront design of the research and development of the consent form or (ii) after a harm had occurred. Accordingly, each of these contexts were the focus of a task on Day 1.

To gather experts' opinions on these topics, we developed two worksheets comprising a framing narrative (one describing upfront research design and the other an unspecified harm) along with the list of places, including a space for 'other' places that they might identify. We asked experts to complete the worksheets by rating the relevance of each place (scale of 1–5, with 1 as 'not at all relevant' and 5 as 'highly relevant' to deciding which state's laws should apply) briefly explaining their rating. As noted previously, experts first filled out each worksheet individually and then completed one representing their small group deliberations, including noting areas of continuing disagreement.

### *Day 2*

Our second workshop focused on choice of law factors. We identified the following potentially relevant factors that appeared in some form across multiple existing choices of law frameworks:

- Place where the wrong/harm occurred

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22 We originally framed this as 'where the principal investigator of the overall study is located,' but our experts raised questions about whether this meant where the PI lived versus worked. Accordingly, we altered how we discussed this place after Day 1 to reflect the common understanding of the more relevant location.



- The interests/policies of the states with relationships to the research
- The needs of interstate and international systems
- Justified expectations of relevant parties
- Certainty, predictability, and uniformity of results
- Ease of determination and application of the law to be applied

We anticipated that the relevance of each factor might differ depending on context, and thus devised three separate research scenarios. Scenario 1 involved secondary research on a topic that was objectionable to a study participant and arguably fell outside the scope of the broad consent, drawing on elements of the Havasupai case.<sup>23</sup> Scenario 2 involved a research design that reflected a decision not to return genomic results unless they were ‘clinically significant’ and a participant who wants access to all genomic results, against a backdrop of a few states with laws that may create a right to those results. Scenario 3 involved a hacker breaching a research database and posting information on the ‘dark web,’ against a backdrop of a few states with laws that provide an explicit right to sue for breach, plus statutory minimum damages, attorneys’ fees, and costs. (See [Appendix 1](#) for the worksheets with the full scenarios.) We considered multiple scenarios based on our prior work,<sup>24</sup> but, mindful of time constraints and cognitive burden on our experts, proceeded with only three scenarios that best represented features we considered relevant to the choice of law question.

Similar to Day 1, we developed worksheets for each of the three scenarios, asking our experts to score the relevance of each of the choice of law factors (including any additional factors they might identify) in assessing what rights and protections should be afforded to research participants and to provide a brief explanation of their score both individually and in their breakout group. We intentionally asked them to consider each factor separately, rather than as part of an existing framework. We also asked them to identify the precision medicine place (from our first workshop list) that *best* represents where the harm occurs in each of the scenarios.

### Day 3

We presented a summary of our preliminary analysis to check that our understanding rang true to our experts’ thoughts and experiences during Days 1 and 2. Specifically, we compiled the individual and group scores and presented these graphically ([Figures 1 and 2](#) and [Appendix 2](#)). After receiving feedback on the results of the first two workshops, we also solicited feedback regarding areas for future study.

## V. RESULTS

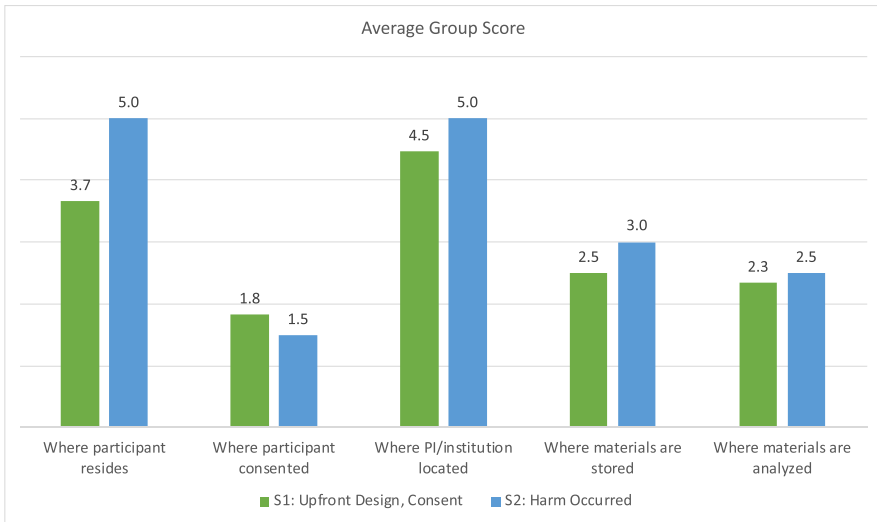
### V.A. Day 1: relevance of place

In our first workshop, we asked for input regarding the relevance of different precision medicine places for choice of law questions. Although we asked our experts to answer

23 Michelle M. Mello & Leslie E. Wolf, *The Havasupai Indian Tribe Case—Lessons for Research Involving Stored Biologic Samples*, 363 N. ENGL. J. MED. 204 (2010).

24 Wolf et al. (2019) and Wolf et al. (2020), *supra* note 1; Beskow et al., (PLOS ONE, 2018), Beskow, et al., (2018) and Hammack, et al., (2019), *supra* note 11.





**Figure 1.** Relevance of Place.

the questions in two contexts—(i) during research design and consent drafting and (ii) after a harm occurred—there was no difference in their answers. For both scenarios, they identified two places as most relevant: the place where the participant resides and the place where the principal investigator/research entity is located (Figure 1).

The groups agreed that *where the participant resides* was relevant because it was where any harm would be experienced. They also mentioned that participants’ background expectations about their rights might be influenced by where they live, as well as states’ interests in protecting participants.

The groups considered where the principal investigator or research entity was located relevant because it was easily determined. They also felt it was fair to hold researchers and their institutions responsible for understanding the laws of their state and may even lead to better governance. Relatedly, groups expressed concern about the burden of holding them responsible for all the different laws where participants live. One group noted that, because the principal investigator directs the research endeavor, one could argue that any harm that occurs could be said to emanate from that location, further supporting this relevance of this place.

One group initially favored where the participant resides as the most relevant place, based on a perceived need for the research to be participant-centered and trustworthy. However, as their conversation continued, the group shifted to favoring where the principal investigator or research entity was located because it would result in more uniformity and consistency and limit the burden on research. They noted that the goals of participant-centeredness and trustworthiness could be met by other means, including transparency about what the rules were during the consent process.

Our experts generally considered where the biospecimens or data are stored and where the biospecimens or data are analyzed somewhat irrelevant. While the location of the biospecimens or data could be considered the location of (potentially) harmful conduct, the location of the principal investigator or research entity was considered

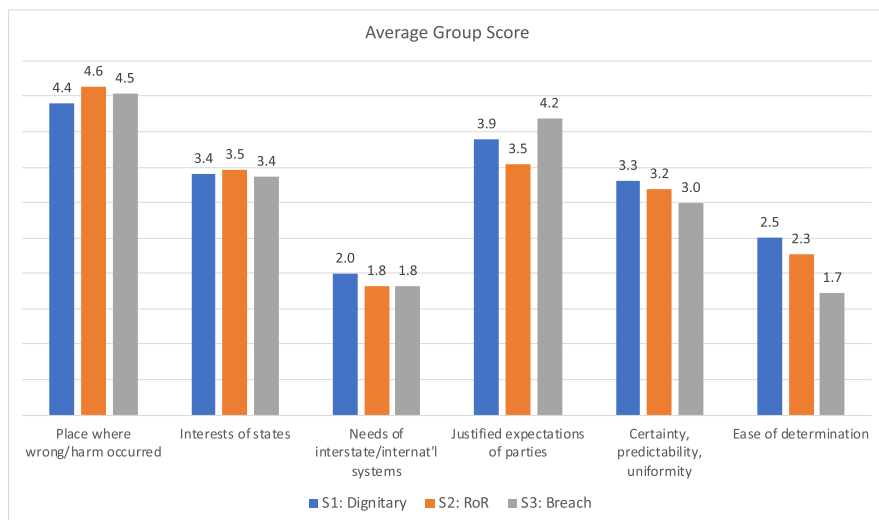
the stronger option. That much data are now electronic and may not physically exist anywhere further supported this assessment for some groups. Some also mentioned that the laws relevant to these places are more about laboratory quality and safety, rather than participant protections. However, one expert pointed out the role of data access committees in determining who has access to the biospecimens and/or data collected in precision medicine research and for what purposes; to this extent, the location of the data access committee (which was not on our original list) may be relevant.

The place where consent was obtained was considered irrelevant by all, a consensus that only grew as groups discussed it. Our experts pointed to how ubiquitous electronic consent has become, which renders the importance of this ‘place’ meaningless. As an analogy, one expert noted that, in general, states have moved away from the place of contract for choice of law purposes.

Despite this overall agreement about the irrelevance of places other than the participant’s residence and the location of the principal investigator or research entity, our experts noted that the type of harm that has occurred might alter their views. They also raised other issues. Multiple choices of law experts pointed out the importance of the content of the law in choice of law questions. Who is being protected and from what has an influence on choice of law determinations, in part, because the content of the law reflects the state’s interests. Laws that are more protective, particularly of participants, might get more weight. Some experts were not concerned that participants may have different rights and protections based on the state where they live because those differences are inherent to our governmental system and may have value. In contrast, others considered fairness and equality as important concepts to strive for and expressed a desire for a federal law that could provide more uniform and coherent protection. A federal law could also resolve some of the other challenges our experts identified, such as the longitudinal nature of precision medicine research; if there were a federal law, it would not matter that the individuals, research entities, data, or specimens could all move over the course of time. It could also mitigate the potential for manipulation, eg, selecting precision medicine research locations to take advantage of more favorable laws. A federal law, however, would not resolve choice of law questions that arise from the international dimension of much precision medicine research (including widespread data sharing); this point was an important reminder that addressing choice of law questions among U.S. states may be only the first step to addressing these issues for research.

### **V.B. Day 2: choice of law factors**

In Day 2 of our workshop, we asked our experts to score the relevance of choice of law factors in assessing what rights and protections should be afforded to participants within the context of three scenarios: objectionable use (#1), return of results (#2), and data breach (#3). There was considerable consistency in scores across the scenarios (Figure 2). The factor of place scored as highly relevant across all three scenarios. Interests of states, justified expectations of parties, and certainty, predictability, or uniformity of results scored as somewhat relevant across all the scenarios, with the exception that justified expectations of the parties scored as highly relevant for the breach scenario (#3). Finally, the needs of interstate or international systems and ease of determination scored as somewhat irrelevant across all three scenarios.



**Figure 2.** Relevance of Choice of Law Factors.

Several experts, particularly choice of law experts, noted that the interests/policies of the states with relationships to the research (reflected in the laws they have adopted) generally receive significant weight in addressing choice of law questions. While appreciating the legal significance of this factor, some research law and ethics experts found less salience from an ethical perspective. Specifically, they expressed concerns that states' economic interests in advancing research may take precedence over participant protections. On the other hand, experts raised examples—such as regulation of medical practice—where states' interests, reflected in positive law, may be protective of participants. Accordingly, reinforcing the discussion in Day 1, choice of law experts suggested that states' interests and the weight they should be afforded depend on the content of the law. For example, one expert noted that sometimes a state writes a law to extend protections to its citizens even for harms that occur outside the state. This unusual approach signals the importance the state places on protecting its citizens from the harm, and, thus, such a law might deserve greater weight. However, others noted the challenge of weighing competing states' interests given the sheer number and distribution of participants and other stakeholders in the precision medicine context.

With respect to the *expectations of the parties*, there was discussion regarding the role of informed consent in setting those expectations. While agreeing with this proposition, some pointed out that there could still be differences in understanding and interpretation between researchers and participants, potentially exacerbated by the knowledge and power differential between the parties. Experience outside of the research context may inform participants' expectations; in particular, experts suggested they may understand the risks presented in the data breach scenario (#3) given how common they have become in daily life (eg, online shopping and banking). Further, participants' wishes may influence their expectations. For example, in the return of results scenario (#2), experts noted that, the participant's desire to have all genomic

results returned conflicted with the research teams' decision not to return results of uncertain clinical significance and may not have been justified. Moreover, as one expert pointed out, 'often times the law disagrees with the expectations of participants,' referring to the *Moore v. Regents of the University of California*,<sup>25</sup> in which the court rejected the research participant/patient asserted ownership rights in his biospecimens that his doctor had commercialized. Some also noted that this factor is somewhat circular 'because justified expectations will usually be based on what the law is'.

Experts described *predictability and uniformity of results* as a goal of all choice of law frameworks, and they similarly recognized its value for the research context. This consensus developed during the small group sessions; choice of law experts tended to score this factor somewhat lower, giving the pragmatic justification that courts do not rely on this factor, whereas research ethics and law experts spoke about its value as a normative principle (Appendix 2). There was some discussion of how some consortia develop principles that will apply to all their research, as an example of how researchers may establish higher standards than local law; nevertheless, these efforts are limited as the consortia cannot extend substantive rights where they are not available. Short of changes to federal regulations to adopt uniform standards that reflect the greater protections afforded by some states, some experts suggested that focusing on the location of the principal investigator might be the best way to ensure that all participants have the same rights and protections. Some considered predictability and uniformity helpful in developing participant understanding and expectations. However, others noted the inherent challenges of predicting what any judge will decide and that reasonable courts can reach different decisions.

In explaining their reasons for scoring it as somewhat irrelevant, choice of law experts stated that, even within their field, there was uncertainty as to what '*the needs of interstate or international systems*' means and that courts rarely use it. Some experts countered this pragmatic approach and found it somewhat relevant for its normative value in facilitating the research enterprise. Some commented that those systemic needs may be more relevant given the nature of precision medicine research, which crosses state lines and involves ubiquitous data sharing as required under federal research policy.

Some considered the *ease of determination and application of the law to be applied* as instrumental, supporting *predictability and uniformity of result*, rather than being particularly relevant as a separate factor. Others viewed these two factors as mutually reinforcing and, thus, independently relevant. That courts pay little attention to the *ease of determination and application of the law to be applied* factor may have contributed to its being scored as somewhat irrelevant.

#### *'Best' place*

We also asked our experts to identify the place that 'best' represents where the harm occurred in each scenario. Although we expected that the preferred place might vary by scenario, the results were consistent with those of Day 1. That is, groups selected *where the participant resides* as the *best* place for two of the scenarios (objectionable use (#1) and return of results (#2)) but mentioned *where the principal investigator or research*

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25 *Moore v. Regents of the University of California*, 51 Cal.3d 120 (1990).

*entity is located* as relevant across all three scenarios and selected it as the *best* place for the breach scenario (#3).

In discussing the objectionable use scenario (#1), experts noted the challenge of identifying the place of harm in the context of a dignitary harm. Although they coalesced around *where the participant resides* as the best place, they commented that the harm may occur elsewhere. For example, if the harm was ongoing, it may be difficult to identify a single best place. They also noted that if the harm were reputational, the harm could be experienced somewhere different from where the participant was living. Others noted the relevance of the *place where the objectionable research was conducted*, as opposed to where the original project was located was more relevant. The place where the offending research was published was also suggested as potentially relevant, although, like precision medicine research, many ‘places’ could be considered the place of publication. Some suggested laws developing around internet-based harm, including bank fraud and other electronic crimes, might provide helpful analogies for locating the harm for choice of law purposes.

In discussing the return of results scenario (#2), some found a stronger case for the place *where the participant resides* than for the objectionable use scenario (#1). With respect to the breach scenario (#3), some experts commented that the place *where the principal investigator or research entity were located* would be more relevant if the breach resulted from a failure to follow appropriate security protocols; as posed, with the breach resulting from a hack, the place *where the participant resides* and experiences the harm was considered more relevant. Others suggested they would look to the place the data were stored if it had a law relevant to hacking. That the harm in the breach scenario occurred as a result of an actor (the hacker) from outside of the research altered thinking on the relevant factors for some. Experts suggested this scenario might favor going with the ‘more participant friendly law,’ even if this results in sort of ‘strict liability’ for researchers.

#### *Additional comments*

As in Day 1, our experts had comments that extended beyond the tasks that we set for them. We asked them to focus on state laws that create choice of law questions, but they reasonably noted that there can be conflicting federal and international laws. They also indicated that concerns posed in our scenarios have analogies outside of the research context. For example, the internet shares some relevant features with precision medicine research, including the dispersal of content providers, vendors, and users, and choice of law approaches in that context could inform how to address the choice of law questions in the research context. But the specific context of research, including the limitation on exculpatory clauses, could limit the value of such analogies. Our experts also noted various ways that the problems we presented could be addressed through changes to the law, such as adoption of more uniform protections through federal or model state laws, a federal choice of law approach, development of a new choice of law framework, or eliminating the restriction on exculpatory clauses. As one expert pointed out ‘to state the obvious, choice of law is always relevant when the laws are different. To the extent we have greater uniformity, choice of law is less significant’. This could lead to alternative mechanisms for addressing concerns, eg, through arbitration or other

non-judicial mechanisms. While endorsing efforts to seek changes to existing laws, our experts acknowledged the practical challenges to effectuating such change.

Some experts commented on the value of our research into this choice of law question. One research ethics expert commented that IRBs already face these questions, with an expectation that these will increase in frequency and complexity, but they have little to guide their decision-making. Another pointed out that researchers and research entities owe ethical duties to participants that require answers to these questions, supporting our starting premise that participant rights and protections, including access to remedies, should not vary in the same study based on where participants live.

### V.C. Day 3

The activities that our experts engaged in during the first two workshops necessarily focused on only some of the factors that would be relevant to a future choice of law framework for precision medicine research. Accordingly, during our third workshop, in addition to soliciting feedback on the results reported above, we also solicited feedback on other factors that were *not* incorporated into our discussions as well as future directions.

#### *Additional factors*

We heard repeatedly over the three days of the workshop that the content or substance of the law is important in a choice of law analysis. Experts talked about different dimensions of this factor, including how protective the law is, what type of protection is afforded, what the remedy is, and who is being protected. With respect to the latter, it was suggested that the weight afforded to the law may depend on whether it is protecting the participant, the researcher or research entity, or someone else, such as a pharmaceutical company. In addition, time was raised multiple times as a relevant factor that was not incorporated into our scenarios. Given the longitudinal nature of precision medicine research, the determination of where the participant resides, where the principal investigator or research entity is located, or where the biospecimens or data are located is complicated by the fact that each of these could move over the course of the study.

Our discussion focused primarily on the research participants and the principal investigator or research entity and the entities storing or analyzing biospecimens and data. However, our experts pointed out there may be other actors, such as funders, industry, patient groups, and the public, whose involvement and/or interests could be relevant to choice of law decisions. They also underscored the complexity of precision medicine research and the choice of law issues it raises; one noted the ‘many different connections, simultaneously [across] so many different places’ challenged their usual approach to choice of law problems. In addition to the state laws we focused on, one expert opined that ‘it would be useful to also bring federal law into this [discussion] because the federal-state conflict brings up a lot of issues’ and another noted that ‘the differences among sovereign nations is just as important as the federal issues’. They also noted that there is not always a clear line between research and clinical practice, which could pose additional choice of law questions by implicating other relevant laws. Given this complexity, it is not surprising that our experts again expressed the desirability of a federal law to resolve the issue.

### Future directions

We asked about what would be useful to the institutional review boards that must review and approve precision medicine research projects (including informed consent processes) before they begin, to researchers who carry out the studies, and the individuals who would like to contribute to research but not take on disproportionate risk. In considering that question, we asked about what data, information, or steps would be necessary to get there, as well as the specific options that might be available.

In response, our experts affirmed the importance of the inquiry. One expert noted that IRBs do confront questions about which laws apply but lack guidance to help them. Thus, anything that could help IRBs address these issues, as well as assist researchers and ultimately benefit prospective and enrolled participants, would be welcome.

As one expert pointed out, the potential options for addressing choice of law questions in precision medicine research will depend on whether ‘the goal is just to sort out how to think about what the jurisdictions might be or is the goal a more aggressive one to try to find some way to channel it toward some cohesive choice of law’. One expert wondered whether the limitation on exculpatory clauses could be overcome through guidance out of the Office for Human Research Protections (OHRP), the agency overseeing the Common Rule or the Food and Drug Administration (FDA), which has its own regulations governing human subject protections, that ‘a choice of law provision in a consent form, which presumably would also have to be . . . in the clinical trial agreement or in the protocol . . . would not be construed as a waiver of rights [but rather as] refining rights or solidifying rights’. This approach, the expert suggested, could address the choice of law problem without eliminating the prohibition on exculpatory clauses altogether. As another expert noted, this approach is arguably consistent with OHRP guidance that statements in consent forms that participants will not receive compensation if their biospecimens are used to develop a commercial product are not exculpatory. The rationale is that participants do not have property rights to their biospecimens and, thus, are not waiving rights. But experts questioned whether that rationale still holds now that some states have adopted laws granting property interests in individual DNA and biospecimens,<sup>26</sup> calling into question the availability of this approach given the various substantive rights and protections state law affords participants. Some also expressed concern that including a choice of law clause in the consent form could be a mechanism for researchers to manipulate the system in ways that disadvantage participants.

Other options suggested as a way forward included a federal law that would provide expanded, uniform protections to participants or a model state law that could encourage greater uniformity among states. Another suggested approach was to ‘have a uniform choice of law approach in how to deal with the problem’. Unless and until such laws were adopted, a comprehensive database that not only collected relevant laws but also provided guidance as to how to determine which laws would apply when could help

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26 Department of Health and Human Services Office for Protection from Research Risks, *Exculpatory Language in Informed Consent Documents: Examples of Acceptable and Unacceptable Language* (OPRR Letter, 1996) (1996), <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/exculpatory-language-in-n-informed-consent-documents/index.html>; Wolf, et al., HEALTH MATRIX, (2019) *supra* note 1; Jessica L. Roberts, *Genetic Conversion*, <http://dx.doi.org/10.2139/ssrn.3357566> (2019); Jessica L. Roberts, *Progressive Genetic Ownership*, 93 NOTRE DAME LAW REV. 1105 (2018).



inform study design and oversight. In advancing attention to choice of law questions in research, one expert opined that ‘it could be useful if you could tie [this idea for greater uniformity or guidance] to the ongoing desire to have a more efficient IRB process,’ a desire that resulted in the single IRB requirement.

Our experts acknowledged the challenges of advancing our research on choice of law issues in precision medicine research into practice. As one commented, ‘I’ve noticed throughout my legal career that there is this instinct . . . among lots of lawyers [and] judges to run in the opposite direction when it comes to choice of law . . . We just assume one [state’s] law applies then we don’t even have to do any sort of analysis’. This observation suggests that researchers and IRBs may be even more reluctant to take on this complicated topic. It also led to the suggestion that ‘raising people’s consciousness in terms of the importance of these issues’ may be the initial step. While encouraging future work on the choice of law issues involving international law, another expert also recognized the research needs to be broken down. Acknowledging that ‘Rome wasn’t built in a day,’ he suggested ‘try[ing] to solve the problem domestically, then you learn from that. And then you take [the findings] to the next harmonization conference. And then you take that to international law’.

## VI. DISCUSSION

Despite the considerable expertise of our experts, our workshops represented the first time that most of them had considered choice of law questions in the research context in depth. Yet one expert confirmed what we already knew from personal experience—that large, precision medicine research studies already are confronting these issues but have little to no guidance in navigating them. Accordingly, our demonstrating how choice of law issues may arise in research and the implications for participants’ rights and protections alone is an important contribution from our research.

Our workshops achieved one of our primary goals: our choice of law and research law and ethics experts learned from each other, which positively influenced the direction of their conversation. The discussions elucidated different connections and ideas that led our experts to different responses than they likely would have come to on their own.

The workshops also underscored the complexity of choice of law issues in the research context. We designed the tasks for the workshops to elicit feedback on specific places relevant to precision medicine research and choice of law factors. We found areas of strong consensus. In particular, the high relevance of the ‘place where the harm occurred’ as a choice of law factor and the agreement that where the participant resides and where the research/institution is located as being the most relevant places. Reconciling these competing approaches will be necessary for a future choice of law framework. We did not have time to explore all dimensions of precision medicine research and choice of law decision-making during our workshop. We focused on scenarios and laws identified in our prior work,<sup>27</sup> but there are other scenarios and sets of laws (eg, consumer protection laws) that should be explored in future research. Nevertheless, our process allowed our experts to identify other factors, such as the content of laws and time, that need to be explored and accounted for in future work.

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27 Wolf et al. (2019) and Wolf et al. (2020), *supra* note 1; Beskow et al., (PLOS ONE, 2018), Beskow, et al. (2018). Hammack, et al. (2019), *supra* note 11.

Developing a framework that can appropriately incorporate all these factors and be used by stakeholders will be challenging. For example, given the substantial variation in state law protections, considering the content of laws may point to multiple states and will not result in a coherent, implementable answer, especially in the context of prospective research design and oversight; while it may be easier to apply this factor after an actual harm has occurred, there are multiple dimensions to this factor that must be taken into account. In addition, we focused our attention on differences in state laws that provide additional protections not afforded by federal law. However, our experts noted how much research is conducted globally, which may implicate different factors.

Our experts suggested different options for future work in developing a choice of law framework for the research context. Deciding choice of law questions through the consent form remained a popular, pragmatic choice, despite the Common Rule's prohibition against exculpatory clauses. Experts questioned whether there may be some room for creativity, given, for example, OHRP's guidance on commercialization. However, they also expressed caution, as this option could allow manipulation of the system to the detriment of participants. We have reservations about this approach. As was discussed during the workshop, circumstances have changed since OHRP issued its guidance on commercialization in 1996 that may render this specific guidance inapposite today. That guidance endorsed the then prevailing view that individuals do not have property interests in their cells after they have been taken from their body as articulated by the California Supreme Court in *Moore v. Regents of the University of California*;<sup>28</sup> thus, a statement that there would be no sharing of profits from products developed from a person's cells was consistent with prevailing law. But the conversation has shifted with technological and scientific advances, including the advent of whole-genome sequencing, and a handful of states have since enacted laws creating property interests in DNA.<sup>29</sup> Given the myriad rights and protections afforded by state law to participants, attempting to replicate this approach would deprive at least some participants of substantive rights and protections currently afforded to them. This is the very definition of 'exculpatory'.<sup>30</sup> Our experts suggested other options for further consideration, such as federal law providing uniform research protections similar to those provided by some states, a federal choice of law approach for research to help resolve these issues, and a model state law. They also encouraged deeper exploration of different factors that should inform choice of law decisions in the research context.

Although our workshops were designed to get a relatively small group of prominent individuals with different kinds of expertise to work together, understanding where opinions might differ based on specific type of expertise may be an important area for future research. For example, our workshop discussions indicate that, at times, research law and ethics experts may have been more focused on the normative value of the

28 *Moore v. Regents of the University of California*, *supra* note 21, at 487–489. Other courts took a similar view of rights to biospecimens. See, eg, *Greenberg v. Miami Children's Hosp. Research Inst. Inc.*, 264 F.Supp.2d 1064 (S.D. Fla. 2003), *Wash. Univ. v. Catalona*, 490 F.3d 667 (8th Cir. 2007), *cert. Denied*, 128 S.Ct. 1122 (2008).

29 See Wolf, et al., (2019), *supra* note 1; Roberts (2019) and Roberts (2018) *supra* note 26.

30 The federal regulations provide that 'No informed consent may include any exculpatory language through which the subject or the legally authorized representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.' 45 C.F.R. 46.116(a)(6) (2018) (emphasis added).

different factors, whereas choice of law experts may have emphasized the pragmatic reality of whether and how a court would use a factor. Understanding of why courts have not relied on these may provide insight into how to incorporate the normative principles more effectively into a new framework.

In sum, our workshops provide important, preliminary insights into how to address choice of law issues in the precision medicine research context. It also reinforced the need for additional research to inform policy-making and guidance to address this complex problem.

#### **SUPPLEMENTARY DATA**

[Supplementary data](#) are available at *Journal of Law and the Biosciences* online.

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