



# MEDICAL RESEARCH LAW & POLICY



## REPORT

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### ***Washington University v. Catalona:* Ownership and Use of Biological Materials Collected for Research**

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The recent decision in the case of *Washington University v. Catalona* highlights the long-standing and growing legal controversy over the issues of ownership and uses of biological materials obtained for research purposes.<sup>1</sup> In handing down its recent decision, one of the few judicial opinions dealing directly with these issues, the *Catalona* court sided with the university and sent a definitive signal to the research community: once subjects give informed consent to donate their tissue, blood, DNA, or other biological materials for research purposes through a legally effective informed consent form (“ICF”), they surrender their rights of ownership to direct the use and transfer of their materials, presumably including the right to determine the secondary uses to which their samples may be put. It is for this reason that the *Catalona* opinion is likely to produce a sense of relief for the clinical research community and particularly for academic medical centers. Although much is still unknown (e.g., the implications of divergent state laws, the effectiveness and legality of “exculpatory language” or “tissue donation waivers”), this decision suggests that subjects may

limit research institutions’ ownership rights as to donated biological materials only to the extent of discontinuing their study participation.

#### **Details of Ownership Dispute**

The dispute between William Catalona, M.D., and Washington University arose when the prominent urologist left his post at Washington University for a similar position at Northwestern University and sought to take with him biological materials that he had collected from his patients for the purpose of prostate cancer research at Washington University. Catalona’s primary assertion was that the biological materials belonged to his patients, and since many of them had signed a consent form drafted by him after his departure agreeing to direct their biological materials to him at Northwestern, Washington University no longer retained a legal interest in those materials.<sup>2</sup> Washington University argued that the subjects had willingly and voluntarily signed consent forms by which they had donated their biological materials to the university and that, once the university obtained those specimens, they became university property.<sup>3</sup> Several of Catalona’s patients who joined the suit argued that they had intended the materials to remain in the possession of Catalona for his research purposes.<sup>4</sup>

The ICF and in particular the rules regarding discontinuation of study participation were at the center of the debate. Under the Common Rule, human subjects must give “legally effective consent” to participate in research, and investigators must not exert undue coer-

<sup>1</sup> *Washington University v. Catalona*, Case No. 4:03CV01065-SNL (E.D. Mo. March 31, 2006).

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<sup>2</sup> *Id.* at 12.

<sup>3</sup> *Id.*

<sup>4</sup> *Id.*

cion or influence over potential research subjects.<sup>5</sup> The regulations also require that ICFs include a statement about withdrawal from a study, explaining that:

[P]articipation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.<sup>6</sup>

In addition, ICFs should include information about the consequences of withdrawing from research.<sup>7</sup> As required by federal regulations, Washington University's ICFs made clear that subjects were entitled to withdraw from participation in a study at any time.<sup>8</sup> The brochure accompanying the ICF explained that subjects should contact the investigator to request that tissue no longer be used for research purposes and that, should a subject withdraw from a study, his or her tissue would be destroyed upon request.<sup>9</sup>

Although the federal regulations make express reference to withdrawal from study participation and most ICFs include reference to the right to withdraw, there is little regulatory guidance on withdrawing or directing biological specimens donated while participating in a study,<sup>10</sup> and it is not uncommon for ICFs to remain silent on the issue or to ask subjects to agree to "donate" specimens for unspecified future research. The Washington University ICF signed by Catalona's patients did not contain express language relating to any subject or patient rights to direct future use or ownership of biologic materials. The only option offered to subjects upon discontinuation in the study was the right to request that their materials be destroyed.<sup>11</sup>

### ICF Plays Determinative Role

In deciding the question of ownership, which the court recognized as the central issue in the case, the absence of specific language in the ICF combined with the circumstances surrounding the ICF played a determinative role. The court underscored the details of the ICFs and the circumstances surrounding their signing: the forms clearly stated that subjects were agreeing to participate in medical studies at Washington University; the ICFs typically included statements that the materials were to be used for research purposes and not for patient care; they often stated that subjects could not claim ownership rights to any medical or scientific products that resulted from research involving the donated samples; the words "donate" and "gift" frequently were used; and the forms bore the university logo, required the stamp of the university's Human

Studies Committee, and advised the research participants that Washington University personnel had oversight of certain aspects of the study.<sup>12</sup> Since the ICF made no representations that the subjects would or could retain ownership and since the circumstances surrounding the donation evidenced ownership on the part of the university, the court concluded that the patients had surrendered the right to use or direct their biological materials. By its ruling, the court sent a definitive signal that the ICF will play a significant role in defining ownership rights to donated biological materials.

Taking into account the circumstances surrounding the ICF and without express reference to ownership or secondary uses in the ICF, the court turned to the state's laws of ownership and donation and to the intent of the patients. The court reasoned that the set of circumstances surrounding the ICFs created an inference of present donative intent on the part of the subjects.<sup>13</sup> According to the court, the subjects must have understood that they were consenting to forego ownership of those donated biologic materials.<sup>14</sup> Because the subjects had delivered their materials to the university, which accepted and maintained possession and control over them, according to state law Washington University established ownership rights over the tissues, which included the right to control their use and direction.<sup>15</sup>

Although state law governs issues of ownership and donation, the court relied on two cases from other jurisdictions, *Greenberg v. Miami Children's Hospital Research Institute, Inc.* and *Moore v. Regents of the University of California*, to support its conclusion that Catalona's patients retained no ownership rights in their biological materials. The precedent in this area is thin, and up until now, the *Greenberg* and *Moore* cases were the primary legal authorities on ownership and secondary uses of biological materials donated for research. In *Greenberg*, where patients donated tissues and data to a physician who then used them to obtain a patent, the court refused to find that the patients had retained a property interest in the tissue or in the genetic information they voluntarily had given with no expectation of return.<sup>16</sup> The *Greenberg* court relied on the *Moore* case, in which the California Supreme Court decided that a patient who had portions of his spleen and biological samples removed from his body did not retain an ownership right in those materials, even though they had been extracted without his consent.<sup>17</sup> The *Moore* court acknowledged, however, that, because he did not consent to the removal, he could bring an action for lack of informed consent.<sup>18</sup> The ruling in *Moore* introduced the notion that a patient gives up his ownership interest in his biologic materials once he consents to donate those samples for research purposes, and

<sup>5</sup> 45 C.F.R. § 46.116

<sup>6</sup> *Id.*

<sup>7</sup> *Id.*

<sup>8</sup> *Catalona* at 6.

<sup>9</sup> *Id.* (warning subjects that any research results already obtained could not be destroyed or recalled).

<sup>10</sup> Federal and state regulations regarding hazardous waste often prohibit the transfer of biological samples back to the subject. *Id.* at 10 (citing 29 C.F.R. § 1910.1030 (bloodborne pathogens); §§ 260.200 R.S.Mo., 260.203 R.S.Mo. (infectious waste disposal); 10 C.S.R. § 80-7.101 (infectious waste management)).

<sup>11</sup> The ICF stated that the subjects were agreeing to waive any right to donated body tissues. As discussed below, an ICF that contains a waiver of rights raises separate questions about whether it respects the Common Rule's ban on exculpatory language.

<sup>12</sup> *Catalona* at 5, 18.

<sup>13</sup> *Id.* at 18.

<sup>14</sup> *Id.* at 21-22 (pointing out that there was no testimony by the patient-defendants that they did not read or understand the ICFs and that the forms mentioned "donation" and a waiver of any claim to excised body tissues).

<sup>15</sup> *Id.* at 12, 17-18 (internal citations omitted).

<sup>16</sup> *Greenberg v. Miami Children's Hospital Research Institute, Inc.*, 264 F. Supp. 1064 (S.D. Fla. 2003).

<sup>17</sup> *Moore v. Regents of University of California*, 51 Cal.3d 120, 793 P.2d 479, 271 Cal.Rptr. 146 (Cal. 1990).

<sup>18</sup> *Id.*

Greenberg and now *Catalona* have reinforced that holding.

### Other Factors in Decision

In addition to the evidence of ownership offered by the ICF, the court pointed to Washington University's management of and oversight over research functions, the biological materials, and the facilities that housed them to support its conclusion that the university owned the donated samples. According to the court, the facts clearly demonstrated that the university retained exclusive possession and control over the biological materials: *prima facie* evidence of ownership under Missouri law.<sup>19</sup> Specifically, the university owned, supplied, funded, and managed the GU Biorepository, the university facility in which the materials were stored.<sup>20</sup> In addition, Washington University had complete control over access to the GU Biorepository and use of the materials, and except to the extent of requesting that samples be destroyed upon withdrawing from a study, no patient had any access to his or her samples once they were made part of the GU Biorepository.<sup>21</sup> The court also pointed to Washington University's Intellectual Property Policy, which revealed that any intellectual property, including research property, on which the university expended significant resources or which was funded by a grant administered by the university, was owned by the university.<sup>22</sup> That *Catalona* was at all times an employee of the university, regardless of who was listed as the principal investigator; the research studies were a collaborative effort involving many individuals, all of whom were employees of Washington University; and the university bore all legal risk with respect to the research performed in connection with the GU Biorepository samples were further evidence of control and thus of ownership on the part of the university.<sup>23</sup> For the court, taking these facts together demonstrated the university's exclusive control over the biological materials and related research functions and lent further support to its holding that Washington University owned, and thus had the exclusive right to use and direct the transfer of, the donated samples.

While not specifically mentioned by the court, the result in this decision is consistent with other established institution-centered research practices. For example, industry research sponsors typically enter into clinical trial agreements with the institution, rather than directly with the investigator (although the investigator may acknowledge or co-sign the agreement). Likewise, National Institutes of Health and National Science Foundation grants typically are made to institutional recipients; when an investigator leaves the grantee institution, the *institution* chooses whether to select a new investigator to continue the grant or instead to relinquish formally its interest in the project and allow the funding agency to re-issue the award to the investigator's new employer. Similarly, title to equipment purchased with grant funds vests either in the federal government or in the recipient institution, but never in the investigator. Equipment typically would "follow" a departing investigator only if the institution decided to re-

linquish its interest in the underlying grant. Thus, the result of the *Catalona* decision confirms an institution-based research model that already is well entrenched in other research contexts.

### Exculpatory Language Merits Scrutiny

Aside from the ownership and secondary use issues raised by tissue donation, the *Catalona* case serves as a reminder that research institutions should pay close attention to the use of exculpatory language in their ICFs. A second argument made by *Catalona* was that the presence of "exculpatory language" in the original ICFs, by which subjects agreed "to waive any claim [they] might have to the body tissues [they] donate[d],"<sup>24</sup> violated the Common Rule, rendering the ICFs invalid and the donations negated.<sup>25</sup> Washington University rebutted that neither the regulations nor the Office for Human Research Protections ("OHRP") guidance on which *Catalona* relied was relevant to the issue of ownership and that the OHRP guidance was not legally binding.<sup>26</sup>

Although the Common Rule explicitly prohibits exculpatory language in ICFs, the application of that prohibition long has proven to be a source of debate and uncertainty within the research community. Specifically, under 45 C.F.R. § 46.116, it is clear that institutions are prohibited from including certain exculpatory language in their ICFs:

No informed consent, whether oral or written, may include exculpatory language through which the subject or the 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.<sup>27</sup>

However, the regulations do not answer the question of how far the ban on waivers extends and in particular whether a waiver of property interests in donated materials violates the Common Rule's prohibition on exculpatory language. In a 1996 guidance document, OHRP's predecessor agency, the Office for Protection from Research Risks ("OPRR"), opined on examples of exculpatory language that offended the federal ban on such language, including a provision similar to that used by Washington University: "By consent to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research."<sup>28</sup> Before that, however, a 1989 letter from the director of the Division of Compliance at OPRR concluded that the ban on exculpatory language was "not intended to prohibit the informed subject from making a legitimate donation of his or her cells or future derivatives of those cells."<sup>29</sup> The inconsistency

<sup>24</sup> Complaint for Declaratory Judgment, *Washington University v. Catalona*, Case No. 4:03CV01065-SNL (E.D. Mo. March 31, 2006).

<sup>25</sup> *Catalona* at 20.

<sup>26</sup> Plaintiff's Pre-Hearing Brief at 19-20, *Washington University v. Catalona*, Case No. 4:03CV01065-SNL (E.D. Mo. March 31, 2006).

<sup>27</sup> 45 C.F.R. § 46.116

<sup>28</sup> OHRP Policy Guidance, OPRR, Cooperative Oncology Group Chairpersons Meeting, Nov. 15, 1996: "Exculpatory Language" in Informed Consent, available at <http://www.hhs.gov/ohrp/humansubjects/guidance/exculp.htm>.

<sup>29</sup> Letter from F. William Dommel, Jr., J.D., Director, Division of Compliance, OPRR, to Merel P. Glaubiger, University

<sup>19</sup> *Catalona* at 12-13.

<sup>20</sup> *Id.* at 3, 13.

<sup>21</sup> *Id.* at 13.

<sup>22</sup> *Id.* at 4.

<sup>23</sup> *Id.* at 3-5, 13.

among the OPRR documents and the vagueness of the regulations explain the uncertainty in this area and the debate it produced among the parties in the *Catalona* case, even though neither the regulations nor the OPRR guidance documents on exculpatory language directly address the issues of ownership and study withdrawal.

After considering the Common Rule ban and the OPRR guidance document, the *Catalona* court found that the federal prohibition on exculpatory language did not affect Washington University's legal rights to the biological materials. The court acknowledged Washington University's legal obligation to refrain from using exculpatory language that relieved the university or its employees from liability for negligence or waived subjects' legal rights.<sup>30</sup> Relying on testimony from experts, the court interpreted the Common Rule prohibition as forbidding exculpatory language containing releases from malpractice or other negligence, and since Washington University's ICF contained no such language, the court regarded the university as having satisfied its legal obligations.<sup>31</sup>

The court declined to address the unsettled issue of whether the regulatory ban on waivers of subjects' legal rights also precludes a waiver of property interests in the donated material. Although the defendants pointed out that OHRP offered language similar to that used by the university as an example of exculpatory language, the court sided with the university and found the argument unconvincing on the basis that the OHRP guidance document was mere opinion and not legally binding.<sup>32</sup> Although the central holding of *Catalona* deals

with the issues of ownership and withdrawal from study participation, research institutions should take note of this part of the decision, since the definition of prohibited exculpatory language is rather unsettled and is set forth in regulatory guidance documents, not in statutes or regulations. Therefore, litigants, regulatory authorities, and subsequent courts undoubtedly will take up this issue with even greater interest and concern.

## Conclusion

In an area with scant regulations and case law, the *Catalona* decision has offered the research community guidance on the issues of ownership, use, and transfer of biological materials donated for the purpose of research. In deciding the central question of ownership, the court largely credited Washington University's position that, once the patients donated their biological samples through legally effective consent forms, the university established an ownership interest and the exclusive right to control the samples' use and direction. This conclusion has broad application in the research community, in which the rights of patients and institutions in the expanding area of tissue research long have been questioned. Particularly relevant to research institutions is the court's focus on the absence in the ICF of any specific language regarding subjects' rights to direct future uses of their biological materials. This case signals that ICFs are likely to play a determinative role in defining ownership rights and should serve as a guidepost to research institutions in drafting and implementing their ICFs. Although the ruling in *Catalona* still does not settle the issue of what "donation" language offends the prohibition on exculpatory language, it offers long-awaited guidance in an area with many questions and few answers.

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Counsel, University of California at Berkeley, dated March 21, 1989.

<sup>30</sup> *Catalona* at 20.

<sup>31</sup> *Id.*

<sup>32</sup> *Id.*