UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

IN RE HUMAN TISSUE PRODUCTS LIABILITY LITIGATION	Civ. No. 06-135 MDL No. 1763
THIS DOCUMENT RELATES TO: ALL CASES	**OPINION** **HON. WILLIAM J. MARTINI**

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MARTINI, U.S.D.J.

This multidistrict litigation arises from a criminal enterprise by Biomedical Tissue Services, Ltd. ("BTS") and its principal Michael Mastromarino to harvest tissue from human corpses without obtaining proper consents and following appropriate regulations. The plaintiffs in this litigation include the recipients of processed tissue supplied by BTS as well as those relatives of the deceased donors. The defendants in this litigation include the principals in the criminal operation, the funeral homes that provided BTS access to the corpses, the companies who processed tissue recovered from cadavers by BTS into various medical products, the distributors of the processed tissue products, and the hospitals and medical personnel who transplanted the processed tissue product. Certain of these defendants have jointly moved for summary judgment on the issue of general causation[1] for the various tort claims asserted by the recipient plaintiffs, who allegedly suffered harm from the processed tissue product. The recipient plaintiffs have opposed the motion and filed a cross-motion for summary

[1] General causation refers to whether a substance is capable of causing a particular injury or condition in the general population. *See Perry v. Novartis Pharms. Corp.*, 564 F. Supp. 2d 452, 463 (E.D. Pa. 2008). It is "established by demonstrating, often through a review of scientific and medical literature, that exposure to a substance can cause a particular disease (e.g., that smoking can cause lung cancer)." Mary Sue Henifin, et al., *Reference Guide on Medical Testimony*, *in* REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 439, 444 (Fed. Jud. Ctr., 2d ed. 2000).

judgment. Additionally, the parties have sought to exclude the proposed testimonies of their respective experts on the issue of general causation. For the reasons articulated below, the defendants' motion to exclude the proposed testimony of four of recipient plaintiffs' experts and motion for summary judgment are **GRANTED IN PART** and the recipient plaintiffs' motion to exclude the proposed testimony of six of defendants' experts and cross-motion for summary judgment are **RESERVED**.

I. BACKGROUND [2]

The product at issue in this products liability litigation involve human allografts. Human allografts are comprised of tissue recovered from a cadaver for use in surgical procedures. Under federal law, tissue recovery agencies may procure human organs and tissue from deceased human donors after meeting applicable regulations, including obtaining proper donor consent and screening donors for certain infectious diseases. The tissue recovery agency sends the tissue to processing companies regulated by the U.S. Food and Drug Administration ("FDA"). These processing companies manufacture allografts from the recovered tissue by disinfecting, sterilizing, or both and then package the allografts for distribution to hospitals for use in surgical procedures. The allografts are

[2] These background facts are not in dispute.

transplanted into patients for the treatment of various medical conditions. For example, bone allografts are processed pieces of bone that are transplanted into and incorporated by a recipient and are used for procedures such as spinal fusion surgery.[3]

All of the tissue at issue in this litigation was recovered by the now-defunct recovery agency, BTS. Pursuant to various agreements with tissue processors, BTS was responsible for obtaining valid donor consents, screening donors, providing samples of donors' blood for testing, and adhering to all federal and state regulations governing tissue recovery. The tissue processors manufactured and packaged allografts from the tissue recovered by BTS. These allografts were then distributed to various hospitals and surgical centers by a distributor such as SpinalGraft Technologies, LLC. Thereafter, the allografts were used during surgery and implanted into recipients.

BTS's criminal scheme was discovered in 2005. In September and October 2005, tissue processors announced a voluntary market withdrawal and recall of allograft recovered by BTS. On October 26, 2005, the FDA issued an announcement that identified tissue recovered by BTS as having originated "from

[3] A number of bone allografts in this litigation involved bone paste, bone tissue that has been ground up and subjected to chemical demineralization before being lyophilized or dried. (Hartill Aff. ¶ 11, Oct. 15, 2007 .)

human donors who may not have met FDA donor eligibility requirements and who may not have been properly screened for certain infectious diseases." (Bense Decl. Ex. 63, Oct. 16, 2007.) Thus, the FDA advised testing for certain infectious diseases and stated, "because of the potential lack of proper screening of the tissue donors, some recipients of the tissues may be at increased risk of infections that could potentially be transmitted through tissues." (Bense Decl. Ex. 63, Oct. 16, 2007.) Furthermore, FDA and Center for Disease Control ("CDC") suggested,

> that implanting physicians inform their patients that they may have received tissue from a donor for whom an adequate donor eligibility determination was not performed. While the overall infectious risk is likely low, FDA and CDC recommend that physicians offer to provide patients access to appropriate infectious disease testing. The relevant communicable diseases for which a tissue donor is required to be tested are HIV-1 and 2 (the viruses that cause AIDS), hepatitis B virus, hepatitis C virus, and syphilis.[4]

(Bense Decl. Ex. 63, Oct. 16, 2007.)

In response to the concern regarding the potential for the transmission of

[4] In an updated public notice, the FDA strongly recommended "that health care providers inform their patients who received tissue implants prepared from BTS donors that they may be at increased risk of communicable disease transmission and to offer them testing." (DePalma Cert. Ex. A, Aug. 16, 2006.) Furthermore, the notice explained that although the FDA "believe[d] that the risks from these tissues are low because the tissues were routinely processed using methods to help to reduce the risk of infectious disease, the actual infectious risk is unknown." (DePalma Cert. Ex. A, Aug. 16, 2006.)

blood-borne diseases[5] through BTS-recovered tissue, Medtronic Sofamor Danek USA, Inc. offered free blood tests for those patients who received allografts subject to the FDA recall and distributed by SpinalGraft Technologies, Inc. on November 8, 2005. (Initial Submission of Defs. Medtronic, Inc., Medtronic Sofamor Danek USA, Inc., Spinalgraft Technologies, LLC, and Regeneration Technologies, Inc. 17-18.) The FDA subsequently ordered the cessation of BTS operations and recalled all tissue products recovered by BTS. Several individuals involved in the BTS operation were indicted on February 22, 2006, and certain of those individuals have since pled guilty to crimes related to the unauthorized recovery of tissue and falsification of donor records.

Civil litigation followed the discovery of the criminal scheme. The lead case in this litigation, *Sechtin v. Regeneration Technologies, Inc.*, Civ. No. 06-0135, was filed in the United States District Court for the District of New Jersey on January 9, 2006. On June 21, 2006, the Judicial Panel on Multidistrict Litigation consolidated the cases arising out of BTS's illegal scheme as *In re Human Tissue Products Liability Litigation*, MDL No. 1763, and assigned the litigation to this Court for pretrial proceedings. There are now approximately 353

[5] HIV, hepatitis B virus, hepatitis C virus, and syphilis are blood-borne diseases, or infectious diseases that are transmitted through contact with infected blood. (Hr'g Tr. 8, Sept. 4, 2008.)

federal cases consolidated before this Court, and additional cases are pending in numerous state courts.

These complaints have been brought by both individual plaintiffs and by representatives of putative class actions.[6] Although the complaints contain a range of claims, the complaints can be categorized generally as: (1) tort claims, such as battery, negligence, product liability, breaches of express and implied warranties, emotional distress, and medical monitoring, by those plaintiffs who allege that they have either contracted a disease, or are in fear of contracting a disease, from transplantation of BTS-recovered allografts;[7] and (2) tort claims, predominately alleging emotional distress, by those relatives of decedents whose tissue was recovered by BTS. The pending motions deal with the former category of plaintiffs–those who claim that they have contracted, or are in fear of contracting, infectious diseases from BTS-recovered allografts (hereinafter, "Plaintiffs").

Defendants have argued generally that BTS-recovered allografts are incapable of infecting recipients with certain diseases due to the methods employed by the processing companies to disinfect and sterilize the allografts.

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[6] The Court has not yet addressed the issue of class certification.

[7] The Amended Master Class Action Medical Monitoring Complaint filed on September 15, 2006 lays forth the specific claims by those plaintiffs who are the recipients of tissue recovered by BTS.

(Defs. Regeneration Technologies, Inc., Medtronic, Inc., Medtronic Sofamor Danek USA, Inc., and SpinalGraft Technologies, LLC, Mot. to Dismiss All Pls.' Claims Because RTI's Sterilized Tissue Allografts are Incapable of Transmitting Disease 3.) For example, Regeneration Technologies, Inc. ("RTI"), a tissue processing company, applies the following sequence of processing for bone allografts: tissue debridement and quality evaluation, bone processing, BioCleanse[8] processing, lyophilization ("freeze-drying"), packaging and labeling, and gamma irradiation and sterrad. (Bense Decl. Ex. I, Oct. 16, 2007.) Thus, Defendants argue, even if the recovery agency failed to properly screen donors to minimize the risk of disease transmission, no virus could survive the sterilization process and storage at room temperature for a prolonged period of time. (Defs.' Initial Submission 24-25; Defs.' Mot. to Dismiss 3.)

Pursuant to the Court's duty as the transferee court in this multidistrict litigation, the Court undertook active case management at the outset of this litigation and sought to identify common issues of fact and law in consultation with the parties. After numerous pretrial orders and conferences, Defendants jointly moved to dismiss Plaintiffs' complaints for failure to state a claim on October 20, 2006 ("Science First Motion"). Orders by Magistrate Judge Ronald

[8] The BioCleanse sterilization process is a proprietary process used by RTI.

Hedges refined the subject of the Science First Motion, and the motion was fully briefed on February 16, 2007.

Oral arguments were held by the Court on March 28, 2007, and at that time, the Court reserved on the Science First Motion and indicated its inclination to convert the motion to dismiss into a summary judgment motion on the issue of causation. The Court, therefore, invited the parties to propose questions to be addressed by further briefing and with the benefit of limited discovery. A continuation of the March 28th hearing was held on April 11, 2007, and after considerable input from the parties, the Court settled upon elements of causation as an initial subject for pretrial disposition. The parties were directed to address the following questions:

> (1) Assume bone tissue from a cadaver that has been infected with hepatitis B, hepatitis C, HIV, syphilis, cancer (all types), and prions, and has not undergone any processing, is stored at a temperature of [blank] for [blank] days, can the bone tissue still transmit one of these viruses/diseases to a donee?
> (2) What is the incubation period for hepatitis B, hepatitis C, HIV, syphilis, cancer (all types), and prions?

(Pls.' Letter to the Ct., June 29, 2007.) The Court invited the parties to supplement their initial Science First Motion submissions with additional expert discovery in response to the Court's two proposed questions. The parties conducted limited discovery, including expert depositions, and submitted

supplemental affidavits and supporting documents from their respective experts to the Court. On August 2, 2007, the Court set a briefing schedule for the converted summary judgment motions and motions to exclude the proposed testimony of experts pursuant to Fed. R. Evid. 702 and *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579 (1993).

The two discrete questions of science before the Court focus upon certain common elements of causation in this litigation. These questions do not take into consideration any of the sterilization processes that the tissue processing companies allege were employed in manufacturing the bone allografts prior to distribution. The sterilization procedures would arguably be additional steps in ensuring that the bone allografts do not infect recipients with infectious diseases.[9] Therefore, the Court is mindful that the present motions only assess the potential for the transmission of diseases short of sterilization. At this juncture, the Court is not assessing whether the tissue processing companies' sterilization procedures prevent the transmission of infectious diseases.[10]

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[9] Consistent with the Court's general causation questions, the relevant infectious diseases in this Opinion are restricted to human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), syphilis, cancer, and prion disease.

[10] Even if the Court were to conclude that unprocessed bone allografts are capable of transmitting certain diseases, the Court would then have to determine the effect that the tissue processing companies' sterilization procedures would have on the alleged ability of bone allografts to transmit disease.

II. PROCEDURAL HISTORY

Presently, there are several motions pending before the Court on the identified issues of causation. Defendants jointly filed a motion for summary judgment on October 16, 2007.[11] Plaintiffs opposed Defendants' motion and submitted a Cross-Motion for Summary Judgment on November 21, 2007. As of December 14, 2007, both summary judgment motions were fully briefed.

In addition, Defendants moved jointly to exclude the proposed testimony of four of Plaintiffs' experts, Suzanne Parisian, M.D., John Kowalski, Ph.D., Andrew Klein, M.D., and Cosme Manzarbeitia, M.D., on October 17, 2007. (Docket No. 433.) Plaintiffs opposed Defendants' motion to exclude. Plaintiffs also submitted a motion to exclude the proposed testimony of six of Defendants' experts, Douglas Richman, M.D., Margaret Koziel, M.D., Marion Kainer, M.B., M.P.H., William Rutala, Ph.D., William Jarvis, M.D., and Daniel Kuritzkes, M.D., on December 17, 2007. (Docket No. 542.) Defendants opposed the motion. Both motions to exclude were briefed by January 28, 2008.

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[11] Defendants RTI, Medtronic, Inc., Medtronic Sofamor Danek USA, Inc., and SpinalGraft Technologies, LLC, (collectively, "RTI Defendants") filed the motion on October 16, 2007. The following defendants formally joined RTI Defendants' summary judgment motion and motion to exclude: Tutogen Medical (United States), Inc. (Docket No. 429, 430); LifeCell Corp. (Docket No. 439, 440); Lost Mountain Tissue Bank (Docket No. 446, 447); Zimmer Dental, Inc. (Docket No. 424, 425); English Brothers Funeral Home (Docket No. 423); Hillcrest Medical Center (Docket No.415, 442); and Palmetto Health Alliance (Docket No. 418). The Court refers to these defendants collectively in this Opinion as "Defendants."

On February 27, 2008, the parties informed the Court of their intention to pursue formal mediation pursuant to L. Civ. R. 301.1. Therefore, this Court ordered a stay on all motions pending mediation on March 3, 2008. On June 5, 2008, the Court was informed that the mediation was unsuccessful, and the stay was subsequently lifted.

On September 4, 2008, the Court conducted a day of oral arguments on both parties' motions for summary judgment as well as their respective motions to exclude the proposed testimonies of various experts. Without objection from any of the parties in this litigation, the Court determined that an evidentiary hearing, including additional testimony from the experts, on the motions to exclude was unnecessary as the parties had submitted all relevant evidence in support of their motions.[12] The parties' motions are now properly before the Court.

III. DISCUSSION

A. Defendants' Motion to Exclude the Proposed Testimonies of Plaintiffs' Experts

[12] The Court found that the factual record was sufficient as the parties: (1) had fully briefed their motions to exclude; (2) had the benefit of the experts' depositions; (3) had ample opportunity to respond to the various challenges to the experts' conclusions, analyses, and methodologies, and to explain the experts' methods and opinions; and (4) had the opportunity to submit all relevant support for the experts' opinions including deposition testimony. *See Padillas v. Stork-Gamco, Inc.*, 186 F.3d 412, 417-18 (3d Cir. 1999) (finding that it is within the district court's discretion to determine whether a *Daubert* hearing is necessary). Furthermore, the parties during oral arguments on the motions indicated that no hearing was necessary or desired. (Hr'g Tr. 167, Sept. 4, 2008.)

In concert with the issues raised in Defendants' summary judgment motion, Defendants moved to exclude the proposed testimonies of Drs. Parisian, Kowalski, Klein, and Manzarbeitia regarding the transmission of HBV, HCV, HIV, syphilis, cancer or prion disease through the transplantation of unprocessed human cadaveric bone tissue stored at room temperature for a given period of time. Defendants also moved to exclude the proposed testimonies of Drs. Klein and Manzarbeitia regarding the length of the incubation period, or the time between exposure to and detection of an infection, for HBV and HCV. Defendants argued generally that the proposed testimonies of these experts failed to meet the standards for the admission of expert evidence under Fed. R. Evid. 702 and *Daubert*. Plaintiffs opposed the motion and argued that their experts' opinions satisfied the evidentiary standards for the admission of expert testimony. The motion has been fully briefed along with all supporting documentation.

After conducting a searching review of the parties' submissions and thoroughly considering all of the motions, it is clear to the Court that the central conflict among the parties involves time, not capacity. For the purposes of these motions, there is no genuine conflict among the parties that unprocessed bone

tissue stored at room temperature[13] can transmit HIV, HBV, HCV, syphilis, and cancer. Rather, the real issue before this Court is for what period of time can such bone tissue transmit these diseases–is it a matter of hours, days, months, or years? The parties agree that unprocessed bone tissue stored at room temperature is capable of transmitting these diseases for some initial period of time. The parties diverge, however, on the issue of transmission after thirty days. Defendants contend that the transmission of disease cannot occur after thirty days, and Plaintiffs have sought to extend the period of transmission beyond thirty days. Similarly, with respect to the incubation period for hepatitis and HIV, Defendants contend that HBV, HCV, and HIV infections can be detected within six months, while Plaintiffs argue that the detection of HBV and HCV infection can take up to two years and HIV between six to eight months. Defendants' motion to exclude

[13] The phrase "unprocessed bone tissue stored at room temperature" refers to bone tissue that has been dried prior to storage at room temperature (within an approximate range of 22°C-25°C) for any length of time. The methods of drying bone tissue vary among the tissue processors. RTI dries bone through lyophilization, a freeze-drying "method which removes moisture and permits storage at room temperature." (RTI's Statement of Material Facts in Supp. of Defs.' Mem. of Law in Supp. of their Mot. For Summ. J. ¶ 11.) Tutogen Medical (United States) Inc. ("Tutogen") dries bone through its proprietary Tutoplast system prior to storage at room temperature. (Tutogen's Br. in Supp. of Mot. and Joinder in RTI Defs.' Mot. for Summ. J. ¶ 9.) Although Plaintiffs have argued that RTI's method of lyophilizing bone tissue does not eliminate the infectivity of diseased bone tissue, Plaintiffs have not specifically addressed Tutogen's method of drying bone for storage at room temperature. The Court notes, however, that regardless of the method employed by the tissue processing defendants to prepare bone tissue for storage at room temperature, Plaintiffs maintain that reliable evidence demonstrates that such bone tissue stored at room temperature is capable of transmitting disease beyond thirty days.

challenges whether Plaintiffs' experts have reliably concluded that the diseases at issue can be transmitted beyond thirty days and that the incubation periods for HBV, HCV, and HIV are beyond six months. Thus, the question that the Court is addressing in the present motion is whether Plaintiffs' expert opinions, extending the transmission and incubation periods of these diseases, is based upon reliable scientific and medical knowledge or whether they are based upon subjective belief and unsupported speculation.

1. Standard for Admissibility under Fed. R. Evid. 702

Under the Federal Rules of Evidence, the trial court acts as a gatekeeper in ensuring the relevance and reliability of all expert testimony. *See Pineda v. Ford Motor Co.*, 520 F.3d 237, 243 (3d Cir. 2008). Fed. R. Evid. 702 governs the admissibility of expert testimony, and it provides that:

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.

Rule 702 articulates three fundamental requirements: (1) the expert must be qualified to render his or her opinion; (2) the scientific process or

methodology employed by the expert in rendering his opinion must be reliable; and (3) the expert's testimony must assist the trier of fact. *See Pineda*, 520 F.3d at 244. In short, an expert's conclusion must meet the "trilogy of restrictions on expert testimony: qualification, reliability and fit." *Schneider v. Fried*, 320 F.3d 396, 404 (3d Cir. 2003). The party offering the proposed expert testimony bears the burden of establishing the admissibility of the testimony by a preponderance of the evidence. *See Padillas*, 186 F.3d at 417-18.

Experts are qualified to render an opinion when he or she "possesses specialized expertise." *Pineda*, 520 F.3d at 244 (quoting *Schneider*, 320 F.3d at 404). This qualification requirement is interpreted liberally, and formal education as well as a "broad range of knowledge, skills, and training" may provide the necessary qualifications. *Id.* (quoting *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 741(3d Cir. 1994)). Consistent with this liberal policy of admissibility, courts have been cautioned not to exclude expert testimony merely because the court feels that the expert is not the best qualified or that the expert does not possess the most appropriate specialization. *Id.* (citing *Holbrook v. Lykes Bros. S.S. Co.*, 80 F.3d 777, 782 (3d Cir. 1996)).

The second prong of admissibility under Rule 702 requires a determination of the reliability, or inquiry into the underlying substance, of the expert's opinion. Expert testimony is "admissible so long as the process or technique used in formulating the opinion is reliable," and the principles and methods employed by the expert are applied reliably to the facts of the case. *Id*. at 247 (citing *Paoli*, 35 F.3d at 742); Fed. R. Evid. 702 advisory committee's note. An "expert's opinions must be based on the methods and procedures of science, rather than on subjective belief or unsupported speculation." *Paoli*, 35 F.3d at 742 (citations and internal quotations omitted). Thus, "the expert must have 'good grounds' for his or her belief." *Id*. (quoting *Daubert*, 509 U.S. at 590). These good grounds must support each step of the analysis and "*any* step that renders the analysis unreliable under the *Daubert* factors renders the expert's testimony inadmissible." *Id*. at 745.

In determining the reliability of expert testimony, trial courts have been directed to consider the following *Daubert*-related factors: (1) whether the scientific method or theory can be or has been tested; (2) whether the method or theory has been subject to peer review and publication; (3) the known or potential rate of error when applied; (4) the existence and

maintenance of standards and controls; (5) whether the method or theory is generally accepted in the scientific community; (6) the relationship of the technique or theory to methods or theories which have been established to be reliable; (7) the qualifications of the expert witness testifying based on the methodology or theory; and (8) the non-judicial uses to which the method or theory has been put. *United States v. Mitchell*, 365 F.3d 215, 234-35 (3d Cir. 2003) (listing factors under *Daubert*, 509 U.S. at 593-95, and *United States v. Downing*, 753 F.2d 1224, 1238 (3d Cir. 1985)). These factors, however, are neither dispositive nor exclusive. *See Pineda*, 520 F.3d at 248. Courts are entrusted to examine the reliability of the proffered expert testimony in a flexible manner.

Although the Court's inquiry into reliability is focused primarily "on principles and methodology, not on the conclusions that they generate," the Supreme Court has recognized that "conclusions and methodology are not entirely distinct from one another." *General Elec. Co. v. Joiner*, 522 U.S. 136, 146, 118 S.Ct. 512, 139 L.Ed.2d 508 (1997). A court cannot shy away from at least a limited review of an expert's conclusions "in order to determine whether they could reliably flow from the facts known to the expert and the methodology used." *Heller v. Shaw Indus., Inc*., 167 F.3d

146, 152 (3d Cir. 1999); *see also In re TMI Litig*., 193 F.3d 613, 682 (3d Cir. 1999) (finding that the district court did not abuse its discretion in excluding an expert's conclusion based upon a logical analysis of the expert's testimony). If "there is simply too great an analytical gap between the data and the opinion offered," the Court may properly exclude the expert's testimony as "nothing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert." *Joiner*, 522 U.S. at 146.

Courts, however, should not exclude an opinion merely because there is an absence of literature on the precise issue as long as other factors demonstrate the reliability of the expert's opinion. *See Heller*, 167 F.3d at 154 (a medical expert need not "always cite published studies on general causation in order to reliably conclude that a particular object caused a particular illness" so long as there are good grounds, such as differential diagnosis, for the conclusion). Thus, other courts have found that the lack of scientific studies either proving or disproving the hypothesis of causality is not necessarily fatal to an expert's opinion. *See, e.g*., *In re Ephedra Prod. Liab. Litig.*, 393 F.Supp.2d 181, 188-89 (S.D.N.Y. 2005). Nevertheless,

there must be good grounds for the experts' conclusions, and any gaps between the science and the conclusion must be bridged by scientific or medical knowledge. *See id*. at 189 ("Analogy, inference and extrapolation can be sufficiently reliable" when the proposed expert's conclusion is the "kind that a reasonable scientist or physician would make in a decision of importance arising in the exercise of his profession outside the context of litigation.")

The final prong of admissibility is the helpfulness, or fit. "Fit" in the context of Rule 702 refers to the helpfulness of the expert's testimony in assisting the trier of fact. This helpfulness requires a "valid scientific connection to the pertinent inquiry as a precondition to admissibility." *Daubert*, 509 U.S. at 591-92. The fit of an expert's opinion to the facts before a court "is not always obvious, and scientific validity for one purpose is not necessarily validity for other unrelated purposes." *In re TMI Litig.*, 193 F.3d at 670 (quoting *Daubert*, 509 U.S. at 591).

The fit requirement also bears upon the reliability of the expert's opinions. For example,

> in order for animal studies to be admissible to prove causation in humans, there must be good grounds to extrapolate from animals to humans, just as the methodology of the studies must

> constitute good grounds to reach conclusions about the animals themselves. Thus, the requirement of reliability, or "good grounds," extends to each step in an expert's analysis all the way through the step that connects the work of the expert to the particular case.

Paoli, 35 F.3d at 742-43. Similarly, in *General Electric Co. v. Joiner*, 522 U.S. at 146-47, the Supreme Court held that there was no abuse of discretion when the district court excluded the testimony of experts who concluded that exposure to polychlorinated biphenyls ("PCBs") caused lung cancer in a plaintiff. The experts relied upon animal studies involving the exposure of high levels of PCBs to infant mice. The Supreme Court concluded that the district court properly discounted their opinions as unreliable, because these animal studies "were so dissimilar to the facts presented in [the] litigation." *Id*. at 144-45.

The issue of fit "is one of relevance and expert evidence which does not relate to an issue in the case is not helpful." *Id*. The standard for fitness is "not that high" but is "higher than bare relevance." *Paoli*, 35 F.3d at 745.

In the context of toxic tort and products liability litigation, plaintiffs often require the admission of expert testimony to evidence causation. Where there is little direct evidence proving an expert's conclusions or in a developing area of medicine and science, courts face particular challenges in determining whether the

expert testimony is sufficiently reliable based upon the scientific and medical information presented to the court. Courts have noted that requiring experts to always "cite published studies on general causation in order to reliably conclude that a particular object caused a particular illness" would "doom" all cases where the research on that subject was in its infancy. *Heller*, 167 F.3d at 155. Plaintiffs' experts must nevertheless demonstrate "good grounds" for all aspects of their proposed testimony, including "the methodology, the facts underlying the expert's opinion, the link between the facts and the conclusion." *Id.* (citing *Paoli*, 35 F.3d at 743-45).

With these legal standards in mind, the Court turns to examining whether Plaintiffs have proved, by a preponderance of the evidence, the admissibility of their experts' conclusions that: (1) unprocessed human cadaveric bone is capable of transmitting HIV, HBV, HCV, syphilis, cancer, and prion diseases when stored at room temperature for thirty days or more; and (2) the respective incubation periods for HIV, HBV, and HCV are longer than six months. Plaintiffs have argued in their written and oral submissions to the Court that their evidence would support such a conclusion. Defendants have challenged the admissibility of Plaintiffs' experts and argued that the conclusions of Plaintiffs' experts are not warranted from the available medical and scientific information. After a full

consideration of all of the evidence and arguments submitted by Plaintiffs and Defendants, the Court finds that Plaintiffs have not met their burden under Fed. R. Evid. 702 and *Daubert*.

2. Application of Rule 702 to Plaintiffs' Proposed Experts

In conformity with active case management practices of federal district courts assigned to multidistrict litigations, the Court directed the parties to focus on two issues of general causation: (1) the transmission of HIV, HBV, HCV, syphilis, cancer, and prions; and (2) the incubation period for these diseases. Thus, the experts focused their testimony in answering these causation questions.[14]

As discussed earlier, the essence of the disagreement among parties' experts is not whether unprocessed bone tissue stored at room temperature[15] can transmit certain diseases, but rather, the length of time that such bone tissue can continue to transmit the diseases at issue. Plaintiffs' experts suggest that transmission of disease can occur for a prolonged period of time; and Defendants' experts suggest

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[14] Numerous expert affidavits were submitted in this litigation. In response to the Court's general causation questions, supplemental expert affidavits were submitted on behalf of Drs. Kowalski, Klein, Manzarbeitia, Nystrom, and Parisian. (Letter from Joseph DePalma dated June 1, 2007.) These affidavits attempted to directly address the Court's questions. Thus, these supplemental affidavits are the primary subject of Defendants' motions to exclude. During oral arguments, Plaintiffs additionally referred to affidavits submitted by Robert O'Leary, Ph.D., and Michael Busch, M.D., Ph.D., regarding different initial questions posed by the Court.

[15] The capacity of unprocessed fresh and frozen bone tissue to transmit HIV, HBV, HCV, syphilis, and cancer is not disputed by Defendants for the purposes of these motions.

that such bone can transmit diseases, if at all, for a relatively short period of time. Therefore, Defendants have moved to exclude Plaintiffs' expert opinions to the extent that they propose to opine that: (1) unprocessed bone tissue kept at room temperature for thirty days or longer can transmit HIV, HBV, HCV, syphilis, or cancer; (2) unprocessed bone tissue can transmit prion diseases; and (3) the incubation periods of HBV, HCV, and HIV are longer than six months.[16] (Mem. in Supp. of Defs.' Mot. to Exclude Proposed Test. of Drs. Parisian, Kowalski, Klein, and Manzarbeitia 1-2.)

After a full consideration of the submissions, the Court finds that only certain portions of the proposed testimony of Plaintiffs' experts are sufficiently reliable and helpful. Although Defendants have challenged the admissibility of the experts' proposed testimonies on grounds of all three criteria–qualifications, reliability, and fit, the Court focused its attention on the substance of the proffered

[16] Plaintiffs take considerable issue with Defendants' construction of the Court's proposed questions. They argue that Defendants' limitation of the question to unprocessed bone tissue stored at room temperature for thirty days or more is arbitrary and self-serving. (Pls.' Mem. in Opp. to Defs.' Mot. to Exclude 24; Mem. in Supp. of Pls.' Resp. to Defs.' Mot. for Summ. J. and Pls.' Cross-mot. for Summ. J. 10-11.) Although the Court recognizes that the questions posed to the parties were more general in scope, Plaintiffs misconstrue the purpose of the questions and the burdens of proof established by the motions. The two questions by the Court were intended as mere guideposts for directing the parties' focus to common issues of fact and law. Defendants' motion to exclude and motion for summary judgment are consistent with and fall within the rubric of issues identified by the Court. It is clearly appropriate for Defendants to challenge aspects of Plaintiffs' experts' conclusions that they believe are not reliable. Similarly, Defendants' summary judgment motion appropriately seeks to identify areas that they believe Plaintiffs lack the appropriate proofs.

testimonies.[17] Specifically, the Court examined whether the methodologies by which the experts have reached their conclusions are reliable, and whether those conclusions will assist the trier in resolving issues of fact in this case by a preponderance of the evidence. For the reasons explained below, Plaintiffs' proposed expert testimony is stricken where they seek to opine that: (1) unprocessed bone tissue kept at room temperature for thirty days or longer can transmit HIV, HBV, HCV, syphilis, or cancer; (2) unprocessed bone tissue is a transmitter of prion diseases; and (3) the incubation periods of hepatitis and HIV are longer than six months.

i.) Relevant Medical and Scientific Literature

Before delving into a specific analysis of the experts' opinions, it is instructive to review the medical and scientific literature upon which the challenged Plaintiffs' experts primarily rely. The Court will examine each individual experts' reliance upon these studies in greater detail in the following sections.

There are several initial observations regarding the relied upon literature.

[17] The Court is satisfied that Plaintiffs' experts are generally qualified within the outer limits of qualifications under Fed. R. Evid. 702. The Court, nevertheless, finds their qualifications only marginal and will address its concerns in examining the reliability of the proposed expert opinions.

The Court first notes that an absence of definitive published studies on the issue of general causation need not *per se* disqualify an expert's opinions on general causation so long as there are other factors supporting the reliability of the opinion. *See Heller*, 167 F.3d at 154. Second, the parties agree that there is no study–whether epidemiological, cohort, or case-controlled–which addresses the specific question of whether unprocessed human bone tissue stored at room temperature for thirty days or more is capable of transmitting infectious diseases to a human recipient. (Hr'g Tr. 69, Sept. 4, 2008.) Thus, if general causation is to be established in this litigation, it may only be established through methodologies, other than medical and scientific literature review, or reliance upon other, less pertinent medical and scientific studies and literature requiring extrapolation from the experts.

The corollary to a lack of literature which addresses general causation is that the core *Daubert* factors are not as helpful to the Court in assessing the reliability of the experts' theories. The extrapolations of Plaintiffs' experts, to the extent they suggest that unprocessed bone stored at room temperature for thirty days or longer is capable of transmitting the diseases at issue based upon the existing literature and professional experience, have not been tested, peer-reviewed, published, or widely-accepted. Instead, the Court must consider other

factors of reliability, such as the medical and scientific relationship between the expert's opinion to theories and literature that have been established to be reliable, the qualifications of the expert witness, and the non-judicial uses to which the opinion has been rendered.

In this litigation, Plaintiffs' experts have based their conclusions primarily upon a literature review and have supplemented their literature-based opinions with their professional experiences. (Pls.' Mem. in Opp. to Defs.' Mot. to Exclude 2.) They have not conducted any independent analysis of data from this litigation nor conducted animal or laboratory studies on the issues before the Court. There is also no indication that they treated or performed diagnostic tests on any of the plaintiffs in this litigation. (Parisian Dep. 23-24, 29, 42; Kowalski Dep. 19-24; Klein Dep. 9; Manzarbeitia 187-89, 203-08.) Thus, the Court must discern whether each expert opinion has been adequately supported "at every step" of the analysis by either cited medical literature or from the experts' experiences. *See Paoli*, 35 F.3d at 745.

On the issue of transmission, the challenged Plaintiffs' experts have generally focused on a set of studies that can be grouped for the purposes of the Court's summary into three types: epidemiological studies, animal studies, and laboratory studies. Indeed, Plaintiffs' counsel devoted much of their oral

argument dissecting and evaluating these studies.[18] The Court notes that these studies cannot directly prove general causation, and therefore, Plaintiffs' experts must provide good grounds for extrapolating the results of the studies or incorporating the findings of the literature into their conclusion regarding general causation. In providing good grounds, Plaintiffs' experts must overcome several hurdles for the appropriate use of the summarized literature in support of their opinions that unprocessed, room temperature bone tissue can transmit HIV, HBV, HCV, syphilis, and prions after a certain period of time.

a) Epidemiological Studies

There have been relatively few epidemiological studies on the subject of disease transmission through bone tissue.[19] Epidemiological studies examine the pattern of disease among groups of people and can be an important tool in assessing general causation in a mass products liability litigation. Due to ethical considerations and the dearth of natural experiments, however, epidemiological studies relevant to this litigation are lacking. There are a limited number of naturally occurring and inadvertent studies of disease transmission through bone

[18] Plaintiffs' counsel identified the studies summarized in this section, among others, during oral arguments as the primary studies supporting Plaintiffs' expert opinions. (Hr'g Tr. 106, 117, Sept. 4, 2008.)

[19] Plaintiffs state that there are only seven studies examining the issue of disease transmission through bone tissue implants. (Pls.' Mem. in Opp. to Defs.' Mot. to Exclude 1.)

tissue implantation. Two studies have been cited by several of the parties' experts: (1) a 1992 study by R.J. Simonds, et al. entitled, "Transmission of Human Immunodeficiency Virus Type 1 from a Seronegative Organ and Tissue Donor," published in the New England Journal of Medicine ("Simonds Study"); and (2) a 2005 study by Barna Tugwell, et al. entitled, "Transmission of Hepatitis C Virus to Several Organ and Tissue Recipients from an Antibody-Negative Donor," published in the Annals of Internal Medicine ("Tugwell Study").

The Simonds Study examined HIV transmission through organ, soft tissue, and unprocessed fresh-frozen bone transplants from an HIV infected, but seronegative, donor in 1985. Thirty-five individuals received these organs and tissues. The study observed that all four organ recipients became infected with HIV after transplantation. Three of the four recipients of fresh-frozen bone became infected with HIV, and the one recipient of fresh-frozen bone that tested negative for HIV was the only recipient of bone marrow-excavated, fresh-frozen bone. Thirty-three recipients of lyophilized soft tissue, lyophilized and ethanol-treated bone, or lyophilized and irradiated dura matter tested negative for HIV. The study noted that "recipients of tissues that were avascular or processed by lyophilization, ethanol, extraction, irradiation, or the mechanical removal of blood and hematogenous elements did not acquire HIV infection." After explaining that

the lack of transmission could have been due to either processing or the fact that the tissues were relatively avascular, the study concluded that its "investigation cannot quantitate the risk of acquiring HIV-1 from these processed and avascular tissues, although it suggests that transmission is uncommon."

The Tugwell Study examined HCV transmission from an HCV infected and HCV RNA positive, but HCV antibody negative, donor who had died in October 2000. The study traced thirty transplant recipients.[20] All three of the organ recipients were found to be HCV-infected. Of the twenty-seven tissue recipients, five were found to be infected with HCV. The five infected recipients had received cryopreserved vein, cryopreserved tendon, and fresh-frozen and Allowash-treated[21] tendon with bone. The remaining tissue recipients were HCV negative at least six months post-transplantation including those that received iodine-soaked cornea, cryopreserved skin, or lyophilized, Allowash-treated, and irradiated bone. The study noted that the "investigation suggests that not all tissues carry the same risk for transmission."

b) Animal Studies

[20] There were forty recipients who received organ and tissues, but four were HCV-infected prior to transplants, five had no post-transplantation serum specimens to test, and one was HCV infected with a "genotype 3a" post-transplantation.

[21] Allowash is a type of proprietary disinfection and sterilization process.

There are three animal studies discussed by Plaintiffs' experts: (1) a 1995 *in vivo* study published in Spine entitled, "Simian Immunodeficiency Virus (Human HIV-II) Transmission in Allograft Bone Procedures," by Stephen Cook, et al. ("Cook Study"); (2) a 1995 *in vivo* study published in Clinical Orthopaedics and Related Research entitled, "Retroviral Transmission in Bone Allotransplantation by Jean Nemzek, et al. ("Nemzek Study"); and (3) a 2004 *in vitro* study published in The American Journal of Sports Medicine entitled, "Lyophilization Does Not Inactivate Infectious Retrovirus in Systemically Infected Bone and Tendon Allografts," by Matthew Crawford, et al. ("Crawford Study"). As these studies all involved animal subjects, the experts must extrapolate the results of these studies, and explain why these studies can reliably demonstrate the capacity of bone tissue to transmit disease in humans.

The Cook Study examined the potential for viral transmission through certain types of bone allografts in monkeys. The study found that monkeys receiving fresh bone allografts or allograft bone that was subject to single or double freeze-thaw cycles became infected with the simian version of HIV. Monkeys who received bone allografts that were subject to a double freeze-thaw cycle and then decontaminated with ethanol, however, were disease free after twenty-six weeks. The study concluded from these results that "SIV (HIV-II) can

be transmitted in bone allograft procedures" and that "freeze-thaw cycles and lavaging to remove blood elements may reduce the infectivity of a bone allograft, [but] these methods should not be relied upon to render an allograft safe for transplantation." Furthermore, the study found that bone allografts exposed to ethanol decontamination and a double freeze-thaw cycle "were incapable of transmitting SIV and did not harbor live virus." The study noted its own limitation in extrapolating the results from the study into the human context as "Simian immuniodeficiency virus is known to be very aggressive with virus titers that are much higher than HIV in humans."

The Nemzek Study examined the transmission of the feline leukemia virus (FeLV) through the transplantation of processed feline bone allografts. The long bones of four previously infected donor cats were harvested. These bones were then subjected to three different forms of freezing treatments prior to transplantation: (1) single freeze-thaw cycle; (2) double freeze-thaw cycle; or (3) double freeze-thaw cycle with water flush to remove bone marrow. In the double freeze-thaw cycles, the bones were allowed to thaw for no longer than four hours and were thereafter refrozen. Two weeks after the transplant, the cats were tested for FeLV weekly for six weeks post-transplant. All of the cats implanted with the bone allografts tested positive for FeLV. Thus, the authors concluded that bone

allografts subjected to freezing may have the ability to transmit disease. The study explained that due to similarities with HIV, FeLV "has served as a safe and effective model for" HIV studies, and that the authors believed that the "study provide[d] an appropriately rigid standard for preliminary studies of allograft processing." The study also noted, however, "despite their biologic similarities, a direct comparison of the infectivity of the 2 viruses is not possible and such a comparison can only be inferred" because the viral burden for FeLV in cats is greater than HIV in humans.

As a follow-up to the Nemzek Study, the Crawford Study examined through a controlled laboratory study whether lyophilization inactivated a retrovirus in systemically infected bone and tendon. This *in vitro* study tested the presence of FeLV in feline bone and tendon that had been freeze-dried according to the American Association of Tissue Banks ("AATB") guidelines and stored at room temperature. As a control, fresh-frozen bones were also tested at the same intervals as the freeze-dried bone. The study did not describe the time interval between freeze-drying and testing.[22] Employing extremely sensitive detection methods, no statistically significant difference was found between the freeze-dried

[22] Dr. Kowalski stated that he spoke with Dr. Arnoczky, one of the co-authors of the Crawford Study, and he learned that the tissue was exposed to room temperature after lyophilization for six days before testing. (Kowalski Dep. 75-76.)

and fresh-frozen bone when tested for FeLV. FeLV was used as a surrogate for HIV because FeLV has "a structure and replication cycle similar to that of HIV." The study concluded that "freeze-drying (performed to AATB recommended standards) alone is ineffective in inactivating retrovirus in systemically infected connective tissues." It noted that specific drying and storage temperatures are not provided in the AATB standards and that viral transmissions may be affected by variations in freeze-drying technique. Furthermore, it was noted that the "effect of freeze-drying on viral load was not directly measured," but the study concluded that "it is unlikely that the freeze-drying technique used in the current study (<2% residual moisture content) had any appreciable effect on reducing viral load in the tissues examined."

c) Laboratory Studies

In vitro studies involve the examination of disease "within an artificial environment, such as a test tube." Michael D. Green, et al., *Reference Guide on Epidemiology*, *in* REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 439, 444 (Fed. Jud. Ctr., 2d ed. 2000). These studies are not as helpful as either epidemiological or animal studies because they are conducted outside of a biological environment, and the conclusions of these studies will always remain one step removed from directly proving causation. Nevertheless, they can provide a reliable basis for

medical and scientific opinions as long as their extrapolations are warranted. A number of *in vitro* studies have been discussed by Plaintiffs' experts: (1) a 1990 study published in Clinical Orthopedics and Related Research entitled, "Human Immunodeficiency Virus Cultured from Bone" by B.E. Buck, et al. ("Buck Study); (2) a 1994 study in the Journal of Clinical Microbiology entitled, "Survival of Human Immunodeficiency Virus in Suspension and Dried onto Surfaces," by J. Van Bueren, et al. ("Van Bueren Study"); and (3) a 2005 study published in Biomaterials entitled, "Effects of lyophilization on the infectivity of enveloped and non-enveloped viruses in bone tissue," by Christine Uhlenhaut, et al. ("Uhlenhaut Study").

The Buck Study explored whether HIV could be recovered by culture from cadaveric bone and tendon tissue recovered from persons with AIDS. The authors found that 60% of bone samples from the AIDS-afflicted donors tested positive for HIV after being frozen for four to seventeen weeks, and even 33% of frozen bone, that was later freeze-dried, cultured positive for HIV. The authors concluded that "these experiments demonstrate that HIV resides in bone and, in some cases, is inactivated by freezing. If it can still be cultured after freezing, it is not inactivated by other usual procedures (washing and freeze-drying) employed in tissue banking." The study, however, does not address the loss of infectivity after

the passage of time.

The Van Bueren Study examined the survival of HIV cultures when suspended in various liquid serum and when dried on a glass coverslip. The authors tested the survival of both cell-associated ("CAV") and cell-free ("CFV") HIV cultures suspended in both a standard tissue culture medium containing 10% serum and in 100% serum. The study found that HIV remained infectious suspended in a standard tissue culture medium containing 10% serum at room temperature (20° to 29° C) for several weeks. For 100% serum, the stability of CAV increased, "demonstrating the protective effect of protein." HIV dried onto a glass coverslip "remained infectious for several days," although CAV lost infectivity more than CFV. Although alerting readers that their results "must be interpreted with caution because virus survival can be affected by many factors," the authors stated that the results of the study can be extrapolated to the *in vivo* situation. They concluded that "under our test conditions" loss of infectivity would be around four to eight weeks. They further concluded that HIV "present in many clinical specimens and pillages may lose infectivity within a few days."

The Uhlenhaut Study considered the effect of lyophilization on an enveloped virus, Vesicular Stomatitis virus (VSV), and two non-enveloped viruses Maus Elberfeld virus (MEV) and Porcine parvovirus (PPV). The study found that

freeze-drying native bone matrix suspensions spiked with these viruses reduced the infectivity of VSV and MEV, but did not reduce the infectivity of PPV. Therefore, the authors concluded that "freeze-drying could have a reducing effect on the infectivity of some viruses, but these findings can not be generalized." The study further determined that "freeze-drying does not inactivate retrovirus infectivity completely." The authors, therefore, concluded that "lyophilization is not sufficient as the sole inactivation method regarding virus safety of musculoskeletal transplants" however reduction of infectivity through lyophilization could be used with other methods . . . [and] could provide relatively high virus safety."

d) Studies regarding the Incubation Period

On the issue of the incubation period for hepatitis and HIV, the challenged Plaintiffs' experts rely primarily upon three epidemiological studies involving discrete populations. Two of the three studies peripherally involve the delayed detection of HBV using certain antibody tests in liver transplant recipients. The third study involves delayed HCV antibody detection in a small population of injecting drug users. These studies all suffer from similar leaps in extrapolating the conclusions of these studies to the population at issue in this litigation, recipients of bone allografts and bone paste.

First, a 1997 study, "Transmission of Hepatitis B by Transplantation of Livers from Donors Positive for Antibody to Hepatitis B Core Antigen, by Rolland Dickson, et al. ("Dickson Study") was published in Gastroenterology. The study investigated cases of HBV transmission in liver transplants. The study found that posttransplant HBV infection "occurs at a high rate in recipients of donors with anti-HBc" and noted a delayed detection of the HBV antibody (between two to thirty-seven months) in a limited number of liver transplant recipients.

Second, a 1999 epidemiological study in the medical journal Blood, "Low Levels of Hepatitis C Virus RNA in Serum, Plasma, and Peripheral Blood Mononuclear Cells of Injecting Drug Users During Long Antibody-Undetectable Periods before Seroconversion" by Marcel Beld, et al. ("Beld Article"), examined the accuracy of HCV antibody testing among nineteen injecting drug users. The authors first noted that the time period between HCV RNA detection and HCV antibody detection in the HCV-infected general population was five to six weeks, but in these rare cases, this "seroconversion" period may be extended up to six to nine months. This study found a delayed antibody response to HCV infection experienced by this specific population. Five of these individuals were HIV-infected before seroconversion, and seven of the twelve non-HIV-infected individuals were antibody detectable within two to ten months. The remaining

five non-HIV-infected individuals were HCV antibody negative for thirteen to ninety-four months. It appears, however, that these injecting drug users had "transiently low detectable levels of HCV RNA" prior to detectable HCV antibodies. The authors cautioned that whether their "data can be extrapolated to rarely exposed populations such as blood donor remains unanswered," and therefore, "more studies are needed in subjects other than [injecting drug users] to extrapolate these findings to the general population."

Third, a 2001 epidemiological study, "De Novo Hepatitis B After Liver Transplantation from Hepatitis B Core Antibody-Positive Donors in an Area with High Prevalence of Anti-HBc Positivity in the Donor Population," authored by Martin Prieto et al. ("Prieto Study") and published in Liver Transplantation examined the transmission of HBV through liver transplants. The primary purposes of the study were to assess the risk of HBV infection among liver transplant recipients from a population of donors with a high prevalence of anti-HBc positivity and analyze the risk factors for acquisition of HBV infection from anti-HBc+ donors. In addition to the primary conclusions of the study, the authors noted that "[i]nterestingly, although HBV infection was diagnosed in the majority of recipients within the first year posttransplantation, HBsAg appeared in 2 individuals 2 years after transplantation."

ii.) Dr. Suzanne Parisian

Dr. Suzanne Parisian is a medical doctor with a specialization in pathology. She received her M.D. from the University of South Florida in 1978 and became board certified in pathology in 1989. (Parisian Dep. 10, 18.) Dr. Parisian was employed at the FDA in the medical device evaluation office for approximately four years. During her time at the FDA and in addition to her general duties, she consulted as a forensic pathologist on an incident involving the admittance of a shipment of skin from Russia through customs. (Parisian Dep. 46-47.) She has expertise in FDA policy and has written a book about the FDA, which includes a chapter on the FDA's oversight of human tissue. (Parisian Dep. 44, 52.) Dr. Parisian has been the President of Medical Device Assistance since 1995, and she has also performed legal consulting for approximately ten years. (Parisian Aff. App.1, May 31, 2007; Parisian Dep. 54.)

Plaintiffs proposed to have Dr. Parisian testify on the issue of transmission of viruses, cancer, and prions.[23] Her expert affidavit discusses the evolution of the tissue banking industry, the history, nature, and concern of periodontal and orthopedic allografts, and the risk of viral, cancer, and prion transmissions.

[23] Initially, Dr. Parisian opined extensively on RTI's sterilization process. For the purposes of the Court's analysis of the summary judgment motions, only her Supplemental Affidavit is referenced.

Specifically, Dr. Parisian would offer the following conclusions: (1) to a reasonable degree of medical certainty, viral and bacterial infections can be transmitted through *frozen* bone and tissue allografts stored for a prolonged period of time; (2) to a reasonable degree of medical certainty, infections can also be transmitted from "freeze-dried and stored bone/tissue;" (3) freeze-drying according to AATB recommendations does not inactivate retroviruses, including HIV; (4) despite the lack of studies on the risk of cancer transfer to recipients of allografts, there is a risk that transplanted bone/tissue may trigger pre-malignant and malignant changes in transplanted bone/tissue and cancer in recipients; and (5) adequate donor screening is the most fundamental and well-regarded safety control for tissue banks. (Parisian Aff. ¶¶ 37-39, May 31, 2007.) Her opinions were based upon a survey of medical and scientific literature as well as her familiarity with the field of pathology and the FDA.

Without rejecting the substance of Dr. Parisian's opinion wholesale, Defendants argue that Dr. Parisian's proposed testimony regarding the transmission of disease by room temperature bone is unreliable and inadmissable under Rule 702 and *Daubert*.[24] Specifically, Defendants move to exclude her

[24] For purposes of this *Daubert* motion, Defendants do not challenge Dr. Parisian's first and fifth conclusions regard frozen bone and the need for adequate donor screening.

opinion by arguing that: (1) her lack of qualifications on disease transmission by bone tissue impairs the reliability of her opinion; (2) her theory regarding the transmission of disease fails the *Daubert* standard; and (3) her extrapolation of the existing medical and scientific literature in support of her conclusion is not reliable and does not fit the facts of this litigation. The Court agrees in part.

Dr. Parisian conducted a literature survey and relied upon the following literature in arriving at her opinion regarding the transmission of disease in bone: (1) a 1991 laboratory study published in the Journal of Medical Virology by E. Tjotta, et al. ("Tjotta Study") concluding that at an optimum pH solution, the half-life of HIV ranged from approximately twenty-four hours at 37 C° to no significant survival loss over six months at -75 C°; (2) Van Bueren Study; (3) Cook Study; (4) Crawford Study; (5) a 2000 study by Philippe Hernigou, et al. published in Acta Orthop Scand ("Hernigou Study") that assessed the effects of heat and radiation on the survival of HIV in allograft bone; (6) a 2006 study by Carol Bienek, et al. published in Cell Tissue Banking ("Bienek Study") that examined the efficacy of gamma irradiation and ethylene oxide gas sterilization on bone allografts; (7) a 2003 case report by James Trotter in the Journal of Bone and Joint Surgery ("Trotter Study") that identified a case of HCV transmission from an allograft bone transplant where the bone had been soaked in antibiotic alcohol and

detergent prior to freezing; and (8) the Uhlenhaut Study. As described in Section (i), these studies alone cannot support Dr. Parisian's conclusion regarding the transmission of disease in unprocessed, room temperature bone that has been stored for thirty days or more without extrapolations. Although these studies support certain of Dr. Parisian's opinions, the studies universally fail to address the specific question of general causation before the Court, the effect of the passage of time on the infectivity of unprocessed, room temperature bone tissue.

Dr. Parisian's conclusion, to the extent that she purports to opine that HIV, HBV, HCV, and syphilis[25] are capable of being transmitted by unprocessed, cadaveric bone tissue that has stored at room temperature for more than thirty days, is woefully deficit. At no point during either her affidavit or deposition did Dr. Parisian adequately explain how her conclusions could be extrapolated from the results or conclusions of any of the studies. Dr. Parisian stated during her deposition that although there was no one single report upon which she most relied, "I think the one article that's supportive that we talked about is the Trotter, but its not the article, the pivotal article that says, yes, the risk." (Parisian Dep. 231.) In explaining the Trotter Study, Dr. Parisian stated that whether the case

[25] Dr. Parisian stated in her deposition that she could not assess the risk of transmission of syphilis in allografts. (Dep. 254-55.)

report involved bone allografts that had been frozen or freeze-dried was uncertain. (Parisian Dep. 164.) Thus, the report that she pointed to as most supportive of her opinion involved a speculative assumption that the case report involved freeze-dried, not frozen bone.

Her explanations of the other referenced studies were similarly unhelpful. With regards to the Cook Study of frozen simian bone and Crawford Study of feline cat bone, she merely noted that SIV and FeLV have been used in other studies as a model or suitable surrogate marker for HIV, without explaining why the results in these studies would be sufficient for extrapolation into the human context. (Parisian Dep. 135, 144.) Further undermining the Court's confidence in her extrapolation from these studies, the authors of the studies expressly note the difficulties in applying the results of these animal studies to humans without further study. Dr. Parisian's discussion of the Tjotta Study (examining the preservation and loss of infectivity of HIV in serum within a laboratory setting), Van Bueren Study (examining the infectivity of HIV suspended in serum and dried on a coverslip within a laboratory setting), Hernigou Study(examining the effects of heat and radiation on the survival of HIV in allograft bone),[26] Bienek

[26] Dr. Parisian acknowledged that the Hernigou Study was not a study of the effects of lyophilization or the inactivation of "HIV merely by keeping it at room temperature for a period of time." (Parisian Dep. 152.)

Study (examining the efficacy of gamma irradiation and ethylene oxide as sterilizers), and Uhlenheut Study (examining the effect of lyophilization on VSV, MEV, and PPV infectivity) merely articulated conclusions not currently in dispute by Defendants, that freeze-drying alone is insufficient to inactivate viruses entirely, and, absent further explanation from Dr. Parisian, they do not fit the facts of this litigation and are insufficient basis for Dr. Parisian's conclusions.

To be clear, the Court does not question the reliability of the underlying studies, but rather the Court finds Dr. Parisian's extrapolations from those studies to her ultimate conclusion lack the factors of reliability. Her extrapolations from these studies were not tested, were not subject to peer review, and had no known rate of error. Her theory that these studies suggest the existence of general causation as framed in this litigation has not been generally accepted. Furthermore, she has not explained the basis for her extrapolations from *in vitro* studies involving various serum, epidemiological studies involving the transmission of disease in frozen bone, animal studies involving different viruses and whose own authors cautioned further studies for the extrapolation of their results in humans, and studies evaluating other methods of sterilization such as radiation, heat, and oxide gas. At best, her opinion from these studies is nothing more than pure speculation.

Plaintiffs' efforts to salvage her proposed testimony is ineffective. First, the arguments and extrapolations of counsel alone are not sufficient to prove the reliability of the experts' conclusions. If Dr. Parisian was unable to explain why these studies help inform her conclusion regarding the ability of bone allografts to transmit disease, Plaintiffs' counsel cannot fill in the gaps. Second, even if the Court were to accept the Plaintiffs' summaries of the literature cited by Dr. Parisian, they nevertheless fail to link these studies in a way that would suggest Dr. Parisian's conclusion. (Pls.' Mem. in Opp. to Defs.' Mot. to Exclude 8-11.) Thus, Plaintiffs have not bridged the analytical gaps between the medical and scientific evidence and Dr. Parisian's conclusions.

Dr. Parisian discounts the importance of the available medical and scientific literature in the formation of her opinion, and explains that:

> It's actually just knowing some of the limitations of manufacturing and looking at the FDA's documents and the CDC. Really that's more compelling than any one of those particular articles . . . . It has to be all these factors, manufacturing, manufacturing limitations, knowledge of what freeze-drying is supposed to do, so it's all of it.

(Parisian Dep. 231.) Dr. Parisian's theory, and indeed one of Plaintiffs' major contentions, appears to be that donor screening is the most effective method of reducing the risk of disease transmission in the human tissue industry and that anything short of reliable donor screening creates greater risk of disease

transmission since there are "manufacturing limitations." (Parisian Dep. 168-69, 231; Hr'g Tr. 121-22, Sept. 4, 2008.) Without explaining these manufacturing limitations, Dr. Parisian turns in support to statements by the CDC and FDA regarding donor screening and recommending infectious disease testing. She noted that the CDC considers bone allografts safe for human implantation, because bone banks use a combination of donor screening and processing of bone tissue. (Parisian Aff. ¶¶ 8-9, May 31, 2007; Parisian Dep. 168-69.) Based upon the CDC's reliance upon both donor screening and processing to ensure the safety of bone allografts, Dr. Parisian, then, appears to suggests that there is always a risk of disease transmission absent donor screening. The Court finds that such a conclusion is pure speculation and unsupported by any reliable scientific or medical evidence. Additionally, Dr. Parisian relies upon the FDA's recall notice and recommendation for infectious disease testing for BTS-recovered allografts as evidence of the risk of infectious disease transmission from bone allografts. (Parisian Dep. 168-69.) The FDA's recall notice and recommendation for disease testing, however, does not shed any light on the length of time that room temperature bone can transmit disease or definitively prove causation in this litigation. The understandably cautious approaches that the CDC and FDA may take in response to a lack of medical literature or speculative concerns may nudge

one factor of reliability in Dr. Parisian's favor–the non-judicial use of her theory–but, this factor alone is insufficient to render her conclusion reliable.

The Court notes that Dr. Parisian's speculation regarding the CDC's assessment of the safety of bone allografts and interpretation of the FDA's recall notice and recommendation for disease testing fails to fit the challenged general causation at issue in the case–whether unprocessed human cadaveric bone tissue stored at room temperature for over thirty days is capable of transmitting HIV, HBV, HCV, syphilis, cancer, and prions. The question of transmission before the Court *assumes* that the donor screening failed. The fact that donor screening, a method used to additionally ensure the safety of bone allografts, failed in this litigation does not impact Plaintiffs' burden to put forth some reliable affirmative evidence of causation in responding to Defendants' motions.[27]

Although Dr. Parisian's qualifications are sufficient to provide expert testimony under the liberal standards of Rule 702, it bears upon the Court's review of the reliability of her opinion. Dr. Parisian's general, clinical, or other experiential knowledge does little to assist her leap over the chasm of established literature to her conclusion. Her purported speciality is in the FDA. Dr. Parisian

[27] The Court notes that despite the recall notices, recommendations for testing, and potential investigations, neither the CDC nor the FDA has yet reported a case of disease transmission via BTS-recovered allografts. (Hr'g Tr. 80-81, Sept. 4, 2008.)

has very little relevant experiences. During her four years at the FDA, Dr. Parisian never reviewed an application for any product that contained human bone allograft. (Parisian Dep. 56.) Her limited experience in the human tissue industry was involvement in a shipment of skin from Russia. Dr. Parisian has had no clinical pathology work since 1995, and does not attend any professional medical meetings on a regular basis. (Parisian Dep. 31, 33, 42.) She is not a peer reviewer for any medical journal. (Parisian Dep. 43.)

Dr. Parisian lack of professional experience and knowledge of the question of disease transmission through bone and the particular diseases at issue is telling. Prior to this litigation, Dr. Parisian had never been familiar with the studies or articles that addressed the transmission of disease by bone allograft and never had been asked to give a health risk assessment as to the potential for disease transmission through bone allografts. (Parisian Dep. 48.) Her self-professed focus in this litigation "was on the FDA and what the FDA's actions were, so I didn't look at the other literature as much as what the FDA was saying since that tends to be what I'm asked to comment on." (Parisian Dep. 52.)

Even more troubling to the Court, regarding the reliability of Dr. Parisian's opinion in extrapolating from the studies, was that she had a lack of familiarity with much of the basic information regarding HIV. Dr. Parisian was unable to

recall that HIV was part of the retrovirus family or how a retrovirus differed from other viruses. (Parisian Dep. 81-84.) When asked during depositions how HIV replicates, Dr. Parisian stated "I don't recall. And I think they have other experts that are going to be talking about HIV, so I will defer to them." (Parisian Dep. 84.) Dr. Parisian similarly was unable to recall the basic structure and replication of HBV and HCV, and again asserted that "I'm not that [sic] expert for that, either, then I think I will defer to them." (Parisian Dep. 85.) In sum, the factors of reliability clearly weigh against the inclusion of her testimony on the issue of general causation as to the time within which these viruses remain infective in unprocessed bone tissue stored at room temperature as challenged by Defendants.

While not directly challenged by Defendants, there can be no reasonable scientific basis for Dr. Parisian's fourth conclusion on the transmission of cancer. Dr. Parisian states that "it is still early to know the potential risk for transfer of cancer from allografts." (Parisian Aff. ¶ 32, May 31, 2007.) She opines that "there is a basis in science to anticipate" that cancer can be transmitted from donor tissue to recipients from various transplanted tissue including bone marrow. (Parisian Aff. ¶ 32, May 31, 2007.) The only basis for her opinion is a 2001 case report by Karin Berg, "Transmission of a T-Cell Lymphoma by Allogenic Bone Marrow Transplantation," published in the New England Journal of Medicine

("Berg Report"), examining an incidence of bone marrow transplant to determine whether cancer had been transmitted. The authors noted that post-transplantation cancer are "usually associated with exposure to radiation . . . [and] in rare cases, they result from the transfer of neoplastic cells in transplanted tissue." The authors noted that several forms of leukemia and metastatic glioblastoma multiform have been transferred by liver, kidney and bone marrow transplants. Based upon this report, Dr. Parisian stated that post-transplantation cancer are "thought to have been associated with residual cellular elements being exposed to radiation . . . in rare cases the transplanted bone marrow itself may be associated with directly transferring malignant cells to the recipient." (Parisian Aff. ¶ 32, May 31, 2007.) Dr. Parisian's limited experience in identifying and classifying cancer as a pathologist and cooperative involvement in medical therapies for the treatment of cancer, (Parisian Dep. 23-24), does not lend greater reliability to her opinion regarding the transmission of cancer through bone tissue stored at room temperature for thirty days or more.

Finally, Dr. Parisian discusses prion transmission. She cites lectures at the National Institutes of Health about the ability of prions to survive and infect individuals despite the cleansing of surfaces. She then merely states that "[i]n terms of bone, prions are a potential risk from both human donated bone as well as

bovine bone." Without further explanation, her opinion on prions is merely speculative.

In summary, Dr. Parisian's opinions regarding unprocessed bone tissue and paste stored at room temperature for thirty days or more do not appear to meet the second and third parts of the *Daubert* and Fed. R. Evid. 702 inquiry–reliability of methodology and "fit." The Court notes that Dr. Parisian's opinion is derived from a literature review. When proposed expert testimony is not based upon the expert's own independent research, but instead on such a literature review, the party proffering such testimony must "come forward with other objective, verifiable evidence that the testimony is based on 'scientifically valid principles.' One means of showing this is by proof that the research and analysis supporting the proffered conclusions have been subjected to normal scientific scrutiny through peer review and publication." *Daubert v. Merrell Dow Pharm., Inc.,* 43 F.3d 1311, 1318 (9th Cir. 1995). Thus, the Court must analyze the literature itself to examine whether it meets the *Daubert* criteria. The bulk of the information, upon which Dr. Parisian relies, involves frozen, fresh, or irradiated bone tissue.[28] This fails to help the Court in understanding the general issue of

[28] As Dr. Parisian was unaware of whether the Trotter Study involved frozen or freeze-dried bone, the Court cannot find that her conclusion was sufficiently reliable. (Parisian Dep. 164-65.)

causation–whether unprocessed bone that is laid dormant at room temperature for a certain length of time is capable of transmitting disease to the recipient.

Furthermore, Dr. Parisian's reliance upon studies involving the infectivity of HIV in a laboratory setting and suspended/preserved in various mediums, absent an explanation by Dr. Parisian about why those mediums or "test systems" are similar or duplicate the human tissue environment, would also fail to help this Court determine the causation issue with regards to bone tissue transplants.

The only study that arguable encompasses the causation question was an animal study. As described in greater detail below with Dr. Klein's analysis, Dr. Parisian fails to explain how transmission of HIV, HBV, and HCV can be extrapolated from the Crawford feline study other than to state that FeLV is a proxy for HIV. Courts have been reluctant to allow expert testimony based upon animal studies to prove causation in humans unless there are good grounds to extrapolate data and results from animals to humans. *See Paoli*, 35 F.3d at 742-43.

The reliability of Dr. Parisian's opinion on transmission is further undermined by her relative inexperience with the transmission of disease, and more specifically, disease transmission in bone. Dr. Parisian admitted that in this litigation, her focus primarily was on the FDA. (Parisian Dep. 52.)

Therefore, the Court will allow Dr. Parisian to offer some, but not all, of her proposed testimony. The Court finds that her opinion, to the extent that one has been made, regarding the extended length of infectivity of unprocessed, room temperature bone tissue beyond thirty days is insufficiently reliable and purely speculative.[29] Dr. Parisian's opinion regarding the extended period of transmission of HIV, HBV, HCV, syphilis and cancer as well as the transmission of prion diseases through bone tissue must be excluded. With respect to the remaining portions of Dr. Parisian's proposed testimony as outlined in her affidavit, the Court will admit her testimony under Rule 702.

iii.) Dr. John Kowalski

Dr. Kowalski is a microbiologist and holds a Ph.D. in Microbial Genetics from the University of Massachusetts (1975). He is the President of Microgamma,

[29] Whether Dr. Parisian actually proposes to testify, that unprocessed bone tissue stored at room temperature for thirty days or more is capable of transmitting HIV, HBV, HCV, syphilis, and cancer to a recipient, is unclear to the Court from Dr. Parisian's Affidavit. Dr. Parisian merely opines that to a reasonable degree of scientific and medical certainty, "infection can be transmitted from freeze-dried and stored bone/tissue." (Parisian Aff. ¶ 37, May 31, 2007.) Additionally, Dr. Parisian merely notes that the risk of cancer transfer has not been well investigated, but that there is ample "scientific evidence of the risk of cadaveric tissue transplantation to patients treated for life-threatening conditions with cancer obtained from transplanted bone/tissue." (Parisian Aff. ¶ 38, May 31, 2007.) Dr. Parisian failed to clarify: (1) for how long the stored tissue could transmit infection; (2) which infections could be transmitted; and (3) whether she was discussing bone and tissue in the conjunctive or disjunctive. Despite the Court's grave reservations as to the exact substance of Dr. Parisian's proposed testimony, the Court will read Dr. Parisian's opinion expansively to include an opinion regarding Defendants' challenged parameters for the purposes of this motion.

his own consulting company, and a former Chief Scientist of Sterilization Research and Development at Johnson & Johnson. He has worked in the field of sterilization processes for over 25 years, but has never had any experience in the sterilization of bone tissue allografts prior to this litigation. (Kowalski Dep. 12.)

Plaintiffs proposed to have Dr. Kowalski testify on the issue of transmission. Dr. Kowalski opined in his affidavit that: (1) frozen (generally temperature of -70 degrees Celsius) bone can preserve the viability of viruses for long periods of time; (2) as freeze-drying is a well-known process for preserving and stabilizing viruses, "frozen, cleaned, and then freeze-dried" bone tissue is still capable of transmitting viral and prion diseases and cancer. (Kowalski Aff. ¶¶ 10, 12, 14-17, May 31, 2007.) In support of his conclusions, Dr. Kowalski proposed two sub-theories that the microstructure of the bone protects viruses and that the freeze-drying process preserves viruses. (Kowalski Aff. ¶¶ 9, 12, 17, May 31, 2007.) His opinions were based upon a survey of the literature and on his training and experience as a microbiologist.

Defendants challenge not only Dr. Kowalski's qualifications as an expert in this litigation, but they also challenge the substance of Dr. Kowalski's proposed testimony to the extent that Dr. Kowalski suggests that "bone tissue kept at room temperature for thirty days can transmit disease" based upon his failure to meet the

Daubert tests of reliability and fit. Defendants argue that Dr. Kowalski's expertise in the sterilization process is merely adjacent to the subject matter of his testimony—that is, the medical potential of the transmission of disease through bone tissue. Also, Defendants argue that Dr. Kowalski's two sub-theories on the protective matrix and preservation of the disease at issue through lyophilization are not supported by medical literature. The Court agrees in part.

The reliability and "fit" of Dr. Kowalski's opinion suffers from the same issues as Dr. Parisian's opinion in that Dr. Kowalski failed to articulate the scientific and medical rationale for extrapolating the results of the available studies to the set of facts in this litigation. As with Dr. Parisian, the Court starts with the premise that none of the studies referenced by Dr. Kowalski directly addressed the challenged issue of general causation before the Court. Thus, Dr. Kowalski must establish the scientific basis for his extrapolations.

It is clear to the Court that Dr. Kowalski's opinion is merely educated guessing. Dr. Kowalski himself acknowledged that with regard to his references to studies including, Sawyer, Levy, and Van Bueren:

> Those studies, and one central issue in this work is: The lack of correlation between loss of viral infectivity in blood, in bone, versus the loss of viral infectivity in a wide range of different media which is not blood; of course in the cat study it wouldn't be human blood, it would be cat blood. And that makes for a – I think a large difficulty in

> directly extrapolating the results of any of those studies to what happens to virus that's been systemically introduced into bone via blood supply. (Kowalski Dep. 130.)

Aside from this self-recognition regarding the difficulty of extrapolating a conclusion from the available literature, Dr. Kowalski additionally failed to provide explanations for his reliance upon the studies cited in his expert affidavit.

First, regarding the transmission of prions, Dr. Kowalski failed to provide any extrapolation for his conclusion that "the transmission of prion disease after extended room temperature storage is clearly possible." (Kowalski Aff. ¶ 16, May 31, 2007.) Dr. Kowalski only cited as support for this theory a study of blood transfusions in humans transmitting prion disease and a study finding prions in bone marrow of sheep and cows. (Kowalski Aff. ¶ 16, May 31, 2007.) Then, Dr. Kowalski referenced the fact that prion infectivity is impervious to environmental conditions such as cold storage, room temperature processing, and freeze-drying. (Kowalski Aff. ¶ 16, May 31, 2007.) These studies fail to support Dr. Kowalski's opinions regarding prion transmission given that: (1) he provided no explanation for his *ipse dixit* leap from the identification of prions in bone marrow in animals to bone tissue in humans or blood transfusions to bone tissue transplants; and (2) the stability of prions under different environmental conditions does not explain how bone tissue can transmit prion disease in humans. Thus, his opinions

regarding the transmission of prions in human bone tissue transplants are neither reliable, nor fit the facts of this case.

Second, with respect to the transmission of HIV, HBV, and HCV, Dr. Kowalski provided no explanation for his reliance upon certain studies. He failed to link how the Nemzek Study involving frozen cat bone could shed light upon the transmission of these diseases in the non-frozen human bone context. Therefore, the Court is left without any basis to conclude that bone tissue stored at room temperature would produce the same result as frozen bone tissue. The remaining *in vitro* studies suffer from a similar failure to provide a basis for extrapolation into the facts of this litigation: (1) the Sawyer (yellow fever) and Berge (enterovirus) studies entailed examinations of viruses not at issue in this litigation; (2) the Levy (Type C retrovirus) and Scott (pseudorabies virus) studies involved enveloped viruses that were more similar to the viruses at issue in this litigation, but also involved storage in media meant to preserve these viruses; and (3) the Uhlenhaut Study that observed no reduction in viral viability for porcine parvovirus, a non-enveloped virus which Dr. Kowalski conceded was not a model for HIV, through freeze-drying (Kowalski Dep. 92.), but observed reductions of infectivity in freeze-dried bone for VSV, an enveloped virus like HBV, HCV, and HIV.

Dr. Kowalski's attempt to provide some depth to his reliance upon the Crawford Study was unpersuasive. Dr. Kowalski stated that he placed "primary reliance on" the Crawford Study because it was "biologically closest to the issue at hand, where we had systemically infected bones in the mammalian system, cats, where the viruses were carried into those bones by blood." (Kowalski Dep. 131-32.) Dr. Kowalski, however, failed to explain why it would be appropriate to extrapolate the results of this particular animal study to the human context. Simply put, the fact that one type of study is closer in model to a human model than another study does nothing more than prove that one or both studies may be inappropriate. Furthermore, the Crawford Study was limited in that it merely examined whether any FeLV-infected cat bone tissue exposed to room temperature after lyophilization for six days tested positive for FeLV. (Kowalski Dep. 75-76.) The study failed to measure the change, if any, of the infection level in the bone, and therefore, Dr. Kowalski was without the means to extrapolate those results beyond the six-day duration of the study.

Additionally, Dr. Kowalski's attempt to extrapolate these studies and his knowledge of microbiology to the facts in this case is unreliable. With respect to his sub-theory that microstructure of the bone protects viruses, Dr. Kowalski admitted that none of his cited references "discusses the residual proteins and salts

from blood remaining the bone microstructure which can result in protective effect for the virus." (Kowalski Dep. 42.) He could not quantify this protective effect, and stated that it was merely a "directional notion." (Kowalski Dep. 42.) He conceded that he could not make a general statement regarding salts as an aid in the preservation of viruses because "each virus may [] well not respond in the same way and there may be interdependencies of salt and protein and other affectors." (Kowalski Dep. 210-11.) Furthermore, he stated that he is not an expert on bone structure and could only explain that bone is different from the "outside of a stainless steel surface" because "bone is a very complex environment with a lot of nooks, crannies and holes for lack of technical term, and opportunities for virus to hide and not have access and be protected, versus simply sitting out on a surface of a – of a solid stainless steel object." (Kowalski Dep. 256-57.) Dr. Kowalski also noted that he had no experience with ensuring the sterility of cadaveric tissue. (Kowalski Dep. 14.) Without the support of any scientific or medical literature or specialized knowledge with regards to bone structure, Dr. Kowalski's belief that bone micro-structure protects viruses amounts to mere speculation.

With regards to the second sub-theory, Dr. Kowalski's proposed testimony is similarly unreliable. Dr. Kowalski conceded that he had found no literature in

direct support of his sub-theory that freeze-drying is used to preserve the infectivity of HBV, HCV, and HIV. (Kowalski Dep. 87-91.) Absent from Dr. Kowalski's proposed testimony is any common link, aside from the fact that they are viruses and not bacterial (Kowalski Dep. 54), between those viruses which can be preserved by lyophilization and the viruses at issue here. Dr. Kowalski's own citation to the Uhlenhaut Study further undermines the reliability of his sub-theory, as the study found that certain enveloped viruses lost infectivity as a result of lyophilization. Furthermore, Dr. Kowalski did not know of any virologists who use freeze-drying to preserve HIV. (Kowalski Dep. 91.) Finally, Dr. Kowalski acknowledged that he was not an expert on HIV. (Kowalski Dep. 146, 253, 257.) Thus, reliance on knowledge outside of the literature does not render Dr. Kowalski's opinion any more reliable.

In essence, Dr. Kowalski's opinion, to the extent that he purports to opine on the ability of room temperature bone stored for more than thirty days in transmitting the diseases at issue, fails to meet the *Daubert* standards. His extrapolations from these studies were not tested, were not subject to peer review, and had no known rate of error. His ultimate theories of general causation and sub-theories have not been generally accepted. As explained at length, there is no reliable scientific basis for his extrapolations. His qualifications, while relevant

and capable of providing more help than the average layperson, lack expertise in the precise area of bone allografts. Furthermore, his conclusions were developed for the purposes of this litigation.

Consistent with the Court's findings regarding the limited reliability and fitness of Dr. Kowalski's expert testimony, the Court will allow Dr. Kowalski to offer some, but not all, of his proposed testimony. Dr. Kowalski's opinion, to the extent that one has been made, regarding the ability of unprocessed bone tissue stored at room temperature for thirty days or more to transmit HIV, HBV, HCV, cancer,[30] and syphilis as well as the transmission of prion diseases through bone tissue is insufficiently reliable and must be excluded.[31] With respect to the

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[30] Dr. Kowalski does not opine that cancer itself can be transmitted through bone tissue. Rather, he argues that the survival of "Epstein-Barr virus, human papilloma virus, hepatitis B virus, hepatitis C virus, human herpes virus 8, and human t-cell leukemia virus" can be causative agents of human cancer. (Kowalski Aff. ¶ 17, May 31, 2007.) As Dr. Kowalski fails to address whether the causative viruses, aside from HBV and HCV, can be transmitted through bone tissue, the Court finds that there is no reliable support for Dr. Kowalski's opinion regarding cancer transmission.

[31] Similar to this Court's reservations with Dr. Parisian, it is unclear from Dr. Kowalski's affidavit whether he intends to opine in favor of the theory that unprocessed bone tissue stored at room temperature for thirty days or more is capable of transmitting the diseases at issue in this litigation. Dr. Kowalski merely notes: (1) "freeze-drying is a well known process for preserving microorganisms, including viruses" and "can survive freeze-drying.;" (2) "prion disease after extended room temperature storage is clearly possible;" (3) "systemically-infected bone that has been frozen, cleaned, and then freeze-dried, is still capable of transmitting viral and prion disease and cancer;" and (4) "infection can be transmitted via bone/tissue that is exposed to a 'process short of sterilization' and has 'been laying dormant for some period of time.'" (Kowalski Aff. ¶¶ 12, 16-17, 22, May 31, 2007.) As Dr. Kowalski fails to address for how long bone tissue stored at room temperature is capable of transmitting disease, these statements are not necessarily incongruous with Defendants' assertions that for the relevant diseases, storage of unprocessed

remaining portions of Dr. Kowalski's proposed testimony as outlined in his affidavit, the Court will admit his testimony under Rule 702.

iv.) Dr. Andrew Klein

Dr. Andrew Klein is a liver transplant surgeon who received his M.D. in 1979 at The Johns Hopkins University School of Medicine, where he specialized in surgery and transplants. Currently, he is a Director at the Comprehensive Transplant Center at Cedars-Sinai Medical Center and is also a Professor of Surgery at the University of California, Los Angeles. Although his specialization in the transplantation of the liver and other organs provides him with significant experience working with transplant patients who have contracted HBV and/or HCV, he has never worked with the transplantation of bone tissue other than to observe the harvesting of bone tissue from a cadaver. (Klein Dep. 6-7.) More than 50% of Dr. Klein's practice involves patients who have been diagnosed with HBV and HCV, and about 5% of his practice involves patients with HIV. (Klein Dep. 21.) He reviewed the files of one patient in this litigation, but he has never treated anyone who had been infected with HBV, HCV, or HIV as a result of a bone graft. (Klein Dep. 9, 14.)

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bone tissue for thirty days or more at room temperature prevents the transmission of disease to recipients. Nevertheless, for the purposes of this motion, the Court will read Dr. Kowalski's affidavit liberally to include Defendants' challenged opinion.

Plaintiffs proposed to have Dr. Klein opine on the issues of transmission and incubation periods of HBV, HCV, and HIV. (Klein Dep. 17-18.) Dr. Klein will testify that these three diseases "can be transmitted through unprocessed cadaver bone and tissue" as well as bone tissue that has been "frozen or freeze-dried for many weeks or months." (Klein Aff. ¶ 3, 10, May 29, 2008.) Furthermore, during his deposition, Dr. Klein opined that the incubation period for HBV and HCV was "two years or greater" from the time when a person has been exposed to when that person will test positive.[32] (Klein Dep. 22.) Specifically, Dr. Klein stated that especially for those patients exposed to HBV from transplanted tissue or organs, can be in "excess of two years," and HCV, in a "number of patient populations," incubation period could be in excess of eighteen months to two years. (Klein Dep. 21-22.) Dr. Klein also opined that the incubation period for HIV was six to eight months. (Klein Dep. 37-38.)

In reaching the transmission conclusion in his Affidavit, Dr. Klein relied primarily on his clinical experience in the field of hepatology and four studies: (1) the Buck Study on HIV, (2) the Nemzek feline study, (3) the Crawford feline study, and (3) the Uhlenhaut study. All of the four studies have been detailed

[32] Plaintiffs state that Dr. Klein's definition of incubation period was the time between exposure and a positive antibody test. (Mem. in Supp. of Pls.' Resp. to Defs.' Mot. for Summ. J. 20.)

earlier in the Court's discussion. In attempting to extrapolate his conclusion from the feline studies, Dr. Klein opined that the basic similarities between FeLV and HIV, such as similar structure, replication cycle, and retroviral designation, as well as the ability to reliably test for FeLV have made FeLV "a well documented and accepted comparative model for the study of HIV." (Klein Aff. ¶ 7, May 29, 2008.) Dr. Klein noted that prior to the Crawford Study, there had been no controlled studies that tested the theory that freeze-drying inactivated infectious viruses. (Klein Aff. ¶ 9, May 29, 2008.) As a follow-on article to the Crawford Study, Dr. Klein stated that the Uhlenhaut Study was a quantitative analysis of the effect of lyophilization on infectivity of viruses, whereas the Crawford Study was a qualitative assessment. (Klein Dep. 84.)

Acknowledging the lack of controlled studies addressing whether frozen or freeze-drying affects the infectivity of HBV and HCV, Dr. Klein further opined that based upon "what we know regarding the relative fragility of the viruses," he believed that it is "reasonable to infer that hepatitis C and hepatitis B viruses will be at least as tolerant to freezing and freeze drying as HIV and FeLV, if not more so." (Klein Aff. ¶ 10, May 29, 2008.) Therefore, Dr. Klein opined that freeze-drying could not be relied upon to prevent disease transmission through allografts, and that "[o]nly through rigorous donor screening, combined with other

processing, can the risk of transmission of disease be substantially reduced." (Klein Aff. ¶ 11, May 29, 2008.)

With regards to the incubation period for HBV and HCV, Dr. Klein again relied upon his clinical experience in hepatology and upon three studies: Beld, Prieto, and Dickson. As described earlier in the Court's discussion, these three studies concluded that the period from infection to detection via antibody testing for HBV in the liver transplant population and HCV among injecting drug users was extended to over two years. (Klein Dep. 26-30.)

Defendants challenge the admissibility Dr. Klein's opinion regarding transmission, to the extent that he purports to suggest that unprocessed bone stored at room temperature for thirty days is capable of transmitting HIV, HBV, and HCV, as well as Dr. Klein's opinion on the incubation periods. Defendants argue that Dr. Klein is not qualified to render his opinions with respect to bone tissue and that his opinions regarding transmission and incubation fail to meet the *Daubert* factors of reliability. The Court agrees in part.

Although Dr. Klein attempted to more fully bridge the gap between the existing literature and his conclusion regarding transmission, the Court is not satisfied that Dr. Klein's extrapolations were reliable or fit the facts of this case. First, the Court notes that his specific conclusions were developed for the purpose

of this litigation. Dr. Klein's extrapolations have not been tested, subject to peer review, or known to have an error rate. He has pointed to no literature that suggests his theory is generally accepted. And, his expertise in hepatology and organ transplants, while relevant in qualifying his general expertise in disease transmission through human tissue, is less reliable in examining the transmission of disease through bone tissue transplants–an area in which Dr. Klein admits his clinical experience is limited to "being present in the operating room when bone was taken from" a cadaver. (Klein Dep. 6-7.) Thus, the central assessment for the Court is whether Dr. Klein's extrapolations have a "sound basis" in science and medicine.

In turning to the substance of his extrapolations, the Court finds that Dr. Klein could not articulate why it is medically or scientifically appropriate to extrapolate the results of the studies upon which he relied to the facts of this case. First, Dr. Klein's cites to the Buck Study as a qualitative test which demonstrated that one human specimen testing positive for HIV after freezing for 18 weeks continued to test positive for HIV upon subsequent freeze-drying. (Klein Dep. 46-47.) This study, however, failed to measure the period from freeze-drying to testing. (Klein Dep. 47.) Thus, the Buck Study can support Dr. Klein's theory that HIV was detected in frozen cadaveric bone that was freeze-dried, but Dr.

Klein's reliance upon the Buck Study in rendering an opinion about the detection of HIV in unprocessed bone tissue stored at room temperature after thirty days is purely speculative. Even if Dr. Klein could establish that HIV was detected in freeze-dried bone stored for thirty days, Dr. Klein has not explained whether the level of HIV detected by the Buck laboratory study could infect a recipient if that freeze-dried bone were implanted. In fact, Dr. Klein foreclosed his ability to make such an inference by describing the Buck study as a qualitative, not quantitative study. As the challenged general causation issue is one of ultimate transmission, the failure of Dr. Klein to support each step in the chain of general causation exposes the lack of reliability.

Second, Dr. Klein's attempt to link the results of the feline leukemia studies by Crawford and Nemzek to HIV in the human context suffers from some of the same issues highlighted with Plaintiffs' other experts. It is not in dispute that FeLV may be similar to HIV in terms of the structure and replication cycle of the virus, and that it has been used by scientists as a model for HIV. (Klein Dep. 92-93.) However, Dr. Klein, admitting that there may be other differences of which he was unaware, was unable to explain those differences other than the fact that FeLV infects cats and that FeLV could be transmitted through saliva. (Klein Dep. 93.) The studies notably did explain additional differences and difficulties in

extrapolating the results of the study to the human context.[33] Furthermore, Dr. Klein fails to explain: (1) how the frozen bone in Nemzek Study assists in the understanding of room temperature bone before the Court, and (2) how to extrapolate the results of the Crawford study when there was no explanation as to the period of time between lyophilization and testing of the cat bone. Dr. Klein further admits that the Crawford study could not determine whether FeLV persisted at an infectious level after lyophilization. (Klein Dep. 191-92.) Thus, Dr. Klein has failed to connect the causal chain of how human infection from transplanted bone allografts can be extrapolated from a study of feline infection from transplanted bone allografts.

Third, Dr. Klein's citation to the Ulhenhaut Study is limited to bolstering the Crawford Study. Dr. Klein conclusion that the three viruses examined in Uhlenhaut were good models in learning about the transmission of HBV, HCV, and HIV were not supported by any medical or scientific evidence. (Klein Dep. 87.) In justifying his theory, he explained without any basis that "these three viruses[,] represent a spectrum of viral attributes[,] is a good methodology to test what happens when you freeze-dry bone." (Klein Dep. 87.) A general statement

[33] The Court may reject experts' attempts to draw conclusions that the authors did not draw. *See, e.g.*, *Soldo v. Sandoz Pharm. Co.*, 244 F. Supp. 2d 434, 506 (W.D. Pa. 2003).

that some viruses which share one attribute, being within the family of enveloped viruses, may retain infectivity after lyophilization, does not necessarily lead to a logical conclusion that the viruses at issue here will retain infectivity after storage at room temperature for thirty days or more.

Finally, Dr. Klein's "reasonable infer[ence]" that HBV and HCV must be able withstand freeze-drying because the HIV virus is more fragile is at best an educated guess. (Klein Aff. ¶ 10, May 29, 2008.) Dr. Klein acknowledges that there are currently no controlled studies testing the survivability of HBV or HCV when subject to freeze-drying. His theory that HBV and HCV will be at least as tolerant to freeze-drying as HIV and FeLV has not been tested or peer reviewed. It appears that Dr. Klein has not expressed such an opinion prior to this litigation, and there is no evidence that such an extrapolation is generally accepted by the medical community. As Dr. Klein is a surgeon and not a virologist and has not treated anyone who was infected with HIV, HBV, or HCV from a bone allograft, his practical experience lends very little reliability to his theory. In light of all *Daubert*-related factors, the Court must conclude that Dr. Klein's proposed testimony regarding the transmission of HIV, HBV, and HCV through unprocessed bone tissue that has been stored at room temperature for thirty days or more is not sufficiently reliable.

Defendants additionally challenge Dr. Klein's proposed testimony regarding the incubation period for HBV and HCV as unreliable under *Daubert* and lacking fit. Dr. Klein's opinion that the incubation periods for HBV and HCV for the population at issue in this case lacks the indicators of reliability. First, Dr. Klein did not direct the Court's attention to any medical or scientific literature suggesting that the incubation period for HBV and HCV, outside of liver transplants and injecting drug users, was over two years. Dr. Klein's theory has not been tested, subject to peer review, and has no known rate of error. Furthermore, as evidenced by the reports of the CDC and FDA recall in this litigation, this theory is not generally accepted in the medical community. Although Dr. Klein appears imminently qualified to render an opinion regarding the incubation period for these diseases in liver transplant patients, his lack of expertise in bone tissue transplants or bone tissue generally bears negatively in the reliability of his opinion.[34] Thus, his attempts to draw upon his own clinical

[34] Dr. Klein stated that liver and cadaveric bone tissue are "not the same thing," although he found them, in the context of the incubation period for detecting HBV antibodies, "analogous in the sense that we're talking about transmission of a virus, of a blood-borne virus." (Klein Dep. 26.) Dr. Klein, however, failed to explain the extent of the analogy in accurately concluding the incubation of HBV in bone transplants. Furthermore, the practice of sourcing and procuring organs for transplant versus bone allograft transplants are different. As Dr. Manzarbeitia explained, organ transplant doctors take tissue from brain-dead cadavers and not from "morgue cadavers." (Manzarbeitia Dep. 223-24.) Then, the procured organs are transplanted within an hour or 75 minutes after circulatory arrest. (Manzarbeitia Dep. 270-72.) The organ transplants must be transplanted within that time frame or else enough cells will die in

experience is unavailing as it relates to liver, not bone, transplants.

Second, Dr. Klein failed to explain how studies involving discrete populations of individuals could be extrapolated to those outside of these discrete populations. Dr. Klein relied upon findings of delayed detection of HBV antibody testing in a limited number of liver and organ transplant recipients in the Prieto and Dickson studies. The Dickson Study, specifically, identified its aim as evaluating the risk of acquiring HBV in liver transplant recipients. In support of his conclusion regarding HCV, Dr. Klein relied upon the Beld article, which found a delayed antibody response to HCV infection experienced by nineteen injecting drug users. Again, there was no attempt by Dr. Klein, other than to suggest that there are some groups of individuals that may experience delayed antibody testing, to explain how the results of studies assessing liver transplants and injecting drug users impact populations outside of the study. In the face of no explanation, the Court can only assume that there are two limited sub-populations of people, liver transplant recipients and injecting drug users, for whom antibody testing for HBV and HCV may not adequately detect infection.

Third, the Court notes that delayed antibody response does not equal lack of

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the organ whereby it is not suitable for transplantation. (Manzarbeitia Dep. 274.) Thus, the procedures for organ versus bone transplants are in many ways not analogous.

ability to detect HBV and HCV infection. Rather, the studies discussed by Dr. Klein dealt with antibody tests versus nucleic acid tests ("NAT"). Dr. Klein acknowledged that NAT testing not only shortened the window of infection detection but also improved the accuracy of test results. (Klein Dep. 152.)

With regards to the incubation period of HIV, Dr. Klein's opinion is similarly unreliable. Dr. Klein opined regarding the incubation of HIV only during his deposition. He stated, " If you're talking about seroconversion with a positive antibody, then you're talking about converting anywhere between four weeks and probably, again six to eight months." (Klein Dep. 37-38.) Although it is questionable whether Dr. Klein's opinion differs materially from the general consensus of Defendants' experts that HIV incubation is at most six months, the Court finds that an opinion by Dr. Klein that HIV incubation is up to eight months is not reliable. This theory has never been tested or subject to peer review. He has pointed to no literature that suggests his theory is generally accepted, and in fact, had no literature even tangentially supporting of his theory. (Klein Dep. 37) ("I didn't have any articles on HIV that deal with this same topic.") Although Dr. Klein claims that the basis of his theory is "just general knowledge" (Klein Dep. 41.), his experiential knowledge cannot be used to bolster his opinion as his expertise is in hepatology and organ transplants, not in virology. (Klein Dep. 44.)

Furthermore, there is no indication that Dr. Klein has ever encountered an incubation period for HIV beyond six months in his practice.

For the foregoing reasons, the lack of fit and reliability of Dr. Klein's conclusions regarding the issues of transmission and incubation beyond the challenged period of time does not meet the standards of Rule 702. His proposed testimony is excluded to the extent that he seeks to opine that: (1) unprocessed human bone tissue stored at room temperature for thirty days or more is capable of transmitting HIV, HBV, and HCV to a recipient; and (2) the period of time between exposure and detection of an infection from HIV, HBV, and HCV is longer than six months. The Court, however, will allow the other opinions expressed in Dr. Klein's affidavit dated May 29, 2006.

v.) Dr. Cosme Manzarbeitia

Dr. Manzarbeitia is another organ transplant doctor. He received his medical degree in 1982 from the Universidad Autonoma de Madrid in Madrid Spain. He specializes in hepatobiliary surgery and liver transplantation. He is the Chairman of the Division of Transplant Surgery and the Director of the Liver Transplant Program at the Albert Einstein Medical Center in Philadelphia as well as an Assistant Professor of Surgery at Thomas Jefferson University School of Medicine. In his practice, Dr. Manzarbeitia has transplanted kidneys, pancreases,

and skin and has also used vein and artery allografts. (Manzarbeitia Dep. 198, 201.) He, however, has never transplanted bone allografts. (Manzarbeitia Dep. 201, 246.)

Plaintiffs proposed to have Dr. Manzarbeitia testify on both the issues of transmission and incubation. In a combination of affidavits and depositions, Dr. Manzarbeitia opined that bacterial and fungal infections, as well as HBV and HCV are "readily transmitted by transplanted tissue because microorganisms can remain viable in such tissue for long periods of time." (Manzarbeitia Aff. ¶¶ 6, 9, Jan. 18, 2006.)[35] More specifically, Dr. Manzarbeitia opined that bone tissue could transmit HBV and HCV for two months or more. (Manzarbeitia Dep. 275.) He further stated that "within a reasonable degree of medical certainty it could potentially transmit it. And I'm talking purely hypotheticals because nobody does that." (Manzarbeitia Dep. 277.) In addition, he opined that tests for HBV and HCV can take up to 12 months to become positive depending on the test used. (Manzarbeitia Aff. ¶ 8, Jan. 18, 2006.) In his deposition, Dr. Manzarbeitia further opined that the incubation period for hepatitis could be up to ten years. (Manzarbeitia Dep. 275-277.)

[35] Dr. Manzabeitia stated that he was not presenting expert testimony on the transmission of prion diseases, cancer, syphilis, or HIV. (Manzarbeitia Dep. 197-98.)

Defendants seek to exclude Dr. Manzarbeitia's proposed testimony regarding both transmission and incubation. Defendants argue that he is not qualified to testify regarding the transmission of hepatitis in bone allograft transplants, and that his opinion on transmission rests upon no reliable scientific or medical evidence and is only *ipse dixit*. With regards to Dr. Manzarbeitia's opinion on incubation, Defendants argue that his opinion is not based on reliable science and do not fit the facts of this case. The Court agrees.

Dr. Manzarbeitia's proposed testimony on transmission has no basis in any specific medical literature and is merely based upon his belief. First, although he stated that his conclusions of the issues were a result of numerous abstracts and literature, he only discussed and produced two studies involving frozen bone, the Trotter Study and a 1995 study by E.U. Conrad, et al., in the *Journal of Bone and Joint Surgery*, during his deposition.[36] (Manzarbeitia Dep. 48, 64, 99.) As Dr. Manzarbeitia is an expert in liver, not bone, transplants, his opinion without support of some specific medical literature regarding transmission of disease lacks sufficient reliability. Second, Dr. Manzarbeitia cites to no data or studies

[36] Since his relative expertise is not in bone tissue transplants, the Court cannot merely rely upon his impression of all of his literature review without the identification and discussion of the studies. To do so, would require the Court to abdicate its responsibilities under Fed. R. Evid. 702 and *Daubert*.

suggesting that cadaveric bone tissue stored at room temperature for more than one month can transmit HBV and HCV.[37] Although he initially relied upon a report from an Australian news show about Korean mummies, he conceded that he did not know whether the viral material detected in the mummy was infectious. (Manzarbeitia Dep. 280.) Third, ultimately, Dr. Manzarbeitia gave as the basis for his opinion that the bone would remain infective at two months that "it is just my opinion." (Manzarbeitia Dep. 284.) This *ipse dixit* fails to meet the reliability standard in *Daubert*.

Dr. Manzarbeitia's suggestion that the structure of bone may protect blood-bourne viruses is similarly without any medical or scientific support. He espoused a theory that the bone matrix may be a privileged site for HCV, but was unable to proffer any specific authorities in support of his theory. (Manzarbeitia Dep. 290.) His explanation for his failure to identify pertinent studies was that "there is not a single article but a conglomerate, the same way that an Impressionist painting is not a single brush stroke but the overall look of the whole picture." (Manzarbeitia Dep. 316-17.) Dr. Manzarbeitia's professional experience is unreliable support for

[37] Dr. Manzarbeitia acknowledged that he did not know the "amount of time where tissue from a cadaver infected with hepatitis B sitting at room temperature . . . would not be able to transmit hepatitis B." (Manzarbeitia Dep. 277.) He stated that the basis of that opinion would require that he "try to extrapolate from existing data and could refer back to . . . [the] existence of virus, especially hepatitis B virus, nuclear material in mummies." (Manzarbeitia Dep. 278.)

his theory given his admission that "bone is not what I deal with on a daily basis." (Manzarbeitia Dep. 288.)

In essence, Dr. Manzarbeitia's failure to supply more than his own opinion in support of his untested, non-peer reviewed, and not generally accepted theory greatly diminishes the reliability of his testimony. Furthermore, Dr. Manzarbeitia's professional knowledge of the transmission of viruses through bone tissue transplants has arisen only out of this litigation. Prior to his retention in this litigation, he had not conducted research or participated in any publications on the transmission of hepatitis by bone allografts. (Manzarbeitia Dep. 221-22.) Thus, to the extent that Dr. Manzarbeitia relies upon his own clinical practice or experience to narrow the analytical gap between science and his theory regarding the transmission of HBV and HCV through bone, his expertise in organ, skin, and vein transplants cannot provide a reliable basis for his opinion.[38]

[38] Although Dr. Manzarbeitia states that his discussion of hepatitis transmission is with "transplantation of full organs," he states that "there is certainly an analogy of transmissibility [sic]" in terms of bone. (Manzarbeitia Dep. 274.) He, however, does not explain why the analogy would be suitable for the facts in this litigation. In fact, Dr. Manzarbeitia admitted that there is a "difference in the likelihood that one type of tissue as compared to another transmit hepatitis" and that the likelihood of transmitting hepatitis through bone tissue allografts is less than organs and other living tissue that he has been involved in. (Manzarbeitia Dep. 222, 225.) Furthermore, Dr. Manzarbeitia conceded that time and temperature are factors that can contribute to the loss of infectivity of viruses. (Manzarbeitia Dep. 225.) Therefore, given that his speciality is in organs and with transplants within a relatively short period of time, the Court finds that his opinions are unreliable and lack fit.

With regards to the incubation period, Dr. Manzarbeitia's theories suffer from similar deficiencies as Dr. Klein. Dr. Manzarbeitia states that the incubation period for HCV or HBV may be "up to twelve months," "six weeks to ten years" and "six weeks and eighteen months to two years with appropriate testing." (Manzarbeitia Dep. 250-252.) Yet, Dr. Manzarbeitia could not cite any medical literature to that effect. (Manzarbeitia Dep. 252-53.) To the extent that he drew upon his experiences from patients who are immuno-suppressed or received full liver or kidney transplants, Dr. Manzarbeitia's opinion with regards to bone tissue neither fits nor is reliable. If Dr. Manzarbeitia intended to extrapolate his experience with organ transplants to bone allograft transplants, he has failed to provide any basis for his extrapolation. Thus, the *Daubert* factors steer this Court to the exclusion of his testimony regarding incubation period for hepatitis for those who received bone transplants.

3. Conclusion on the Admissibility of Plaintiffs' Proposed Expert Testimonies

Within the parameters challenged by Defendants, Plaintiffs' experts have failed to meet the criteria for admissible expert opinion. Although several of Plaintiffs' challenged experts will be permitted to testify as to certain statements, they may not seek to testify as to the transmission of HIV, HBV, HCV, syphilis,

and cancer by unprocessed bone tissue stored at room temperature for thirty days or more as well as the transmission of prion disease generally by bone tissue stored at room temperature. Furthermore, Dr. Klein and Dr. Manzarbeitia's conclusions regarding the extended incubation periods for HIV, HBV, and HCV are excluded.

The Federal Rules of Evidence 702 and the progeny of *Daubert* set forth the district court's gatekeeping role with respect to expert evidence. These guidelines not only charge the trial court with assessing the reliability and helpfulness of the expert evidence, but also grant the court discretion to determine whether expert testimony meets the standards. Based upon the extensive record before the Court, Defendants' motion to exclude the portions of Drs. Parisian, Kowalski, Klein, and Manzarbeitia's proposed testimony regarding the transmission of HIV, HBV, HCV, syphilis, and cancer is granted to the extent that these experts purport to opine that unprocessed human cadaveric bone which is stored at room temperature for over thirty days can transmit these diseases. Their proposed testimony, to the extent that an opinion is made, regarding the ability of unprocessed bone tissue to transmit prion disease in a recipient is also excluded. Furthermore, Defendants' motion to exclude Dr. Klein and Dr. Manzarbeitia's proposed testimonies regarding the incubation periods of HIV and hepatitis as extending beyond six

months are also granted.

B. Defendants' Motion for Summary Judgment

In addition to the motions to exclude expert testimony, Defendants moved for summary judgment on two issues of general causation in this case–transmission and incubation. First, they challenge the sufficiency of evidence supporting plaintiffs' theory of general causation with regards to the transmission of HIV, HBV, HCV, syphilis, and cancer through unprocessed bone tissue that has been stored at room temperature for thirty days or more. Furthermore, Defendants challenge Plaintiffs' general causation theory regarding prions and bone paste in its entirety. Second, they challenge the sufficiency of evidence supporting Plaintiffs' theory that there remains a risk of developing HBV, HCV, HIV, and syphilis after a recipient tests negative for these diseases six months from transplantation of bone tissue or paste. Specifically, Defendants seek summary judgment on: (1) the tort claims of all plaintiffs who allege to have contracted disease from bone tissue stored at room temperature for thirty or more days; (2) the emotional distress claims of all plaintiffs who were allegedly exposed to disease from bone stored at room temperature for thirty or more days and tested negative for disease; and (3) the claims of medical monitoring.

Plaintiffs argue that they have put forth, by way of the proposed testimony

of their experts, sufficient evidence of risk of transmission of these diseases sufficient to create genuine issues of material fact. Furthermore, Plaintiffs have filed a Cross-motion for Summary Judgment on the issue of general causation contending that: (1) disease can be transmitted by frozen and fresh frozen bone allografts; and (2) disease can be transmitted to those who received lyophilized allografts less than thirty days from harvesting. (Mem. in Supp. of Pls.' Resp. to Defs.' Mot. for Summ. J. and Pls.' Cross-Mot. for Summ. J. 49.) The motions have been fully briefed and the Court heard oral arguments on September 4, 2008. For the reasons stated below, the Court will grant in part Defendants' summary judgment motion, and reserve in part. The Court will also reserve on Plaintiffs' cross-motion for summary judgment.

1. Standard of Review

Summary judgment eliminates unfounded claims without recourse to a costly and lengthy trial. *See Celotex Corp. v. Catrett*, 477 U.S. 317, 327 (1986). A court, though, should only grant summary judgment "if the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving party is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(c). In evaluating a summary judgment motion, a court must view all evidence in the light

most favorable to the nonmoving party. *See Matsushita Elec. Indus. Co., Ltd. v. Zenith Radio Corp*., 475 U.S. 574, 587 (1986); *Goodman v. Mead Johnson & Co.*, 534 F.2d 566, 573 (3d Cir. 1976).

The substantive law determines which facts are material. *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 48 (1986). Factual disputes are genuine if a reasonable jury could return a verdict for the non-movant, and "[o]nly disputes over facts that might affect the outcome of the suit under the governing law will properly preclude the entry of summary judgment." *Id.* at 248-49. No issue for trial exists unless the nonmoving party can demonstrate sufficient evidence favoring it such that a reasonable jury could return a verdict in that party's favor. *See id*. at 249.

The burden of showing that no genuine issue of material fact exists rests initially on the moving party. *See Celotex*, 477 U.S. at 323. A litigant may discharge this burden by exposing "the absence of evidence to support the nonmoving party's case." *Id*. at 325.

Where the nonmoving party has the burden of proof, the moving party may prevail by demonstrating that "the nonmoving party has failed to make a sufficient showing of an essential element of her case." *Id.* at 323. The nonmoving party may not rely upon bare assertions or conclusory allegations, but must adduce evidence

establishing that there is a genuine factual dispute for trial. *Fireman's Ins. Co. v. DuFresne*, 676 F.2d 965, 969 (3d Cir. 1982).

2. Uncontested Facts

At the outset, the Court notes certain material issues of fact which are not in dispute in the parties' cross-motions for summary judgment. The parties during oral arguments agreed that there were several undisputed issues of fact in this case. First, HIV, HBV, HCV, and syphilis are blood-borne pathogens. (Hr'g Tr. 8, Sept. 4, 2008.) Second, human cadaveric bones, under certain circumstances, when transplanted into a recipient may transmit these diseases. Specifically, unprocessed and frozen human cadaveric bone is capable of transmitting these diseases into a recipient for thirty days or longer. (Hr'g Tr. 8-9.) Additionally, unprocessed and freeze-dried bone stored at room temperature can transmit these diseases up to thirty days.[39] (Hr'g Tr. 9.) Third, lyophilization alone does not inactivate viruses. (Hr'g Tr. 10.) Fourth, the incubation period with respect to syphilis is less than six months. (Hr'g Tr. 10.) Fifth, viruses kept at room temperature over time will lose infectivity. (Hr'g Tr. 11.)

3. Unprocessed Bone Tissue Stored at Room Temperature for More Than Thirty Days

[39] Defendants argue that thirty days is a conservative estimate. (Hr'g Tr. 9, Sept. 4, 2008.)

The issue of general causation as framed by the Court and challenged by Defendants under Fed. R. Civ. P. 56(b) involves unprocessed bone tissue stored at room temperature for more than thirty days. They argue that Plaintiffs, as the non-moving party with the burden of proof at trial, have insufficient evidence of general causation to prevail as a matter of law.[40] Plaintiffs dispute this allegation and assert that there is sufficient evidence to sustain their claims.

Each party was given sufficient opportunity to present any evidence with regards to this question. Plaintiffs initially submitted expert affidavits from Drs. Suzanne Parisian, Robert O'Leary, Michael Busch, John Kowalski, John Conomy, Cosme Manzarbeitia, J. Scott Nystrom, and Richard Rosa. In response to the Court's focus on the issue of general causation, Plaintiffs submitted supplemental expert affidavits addressing this issue from Drs. Kowalski, Andrew Klein, Manzarbeitia, Nystrom, and Parisian. Defendants generally argue that after the exclusion of Plaintiffs' experts' proposed testimony, Plaintiffs have failed to provide any reliable evidence sufficient to create a genuine issue of material fact.

Plaintiffs advance the proposed testimonies of their respective experts as

[40] In assessing Defendants' motion for summary judgment, the Court does not rely upon any evidence submitted by Defendants' proposed experts as a motion to exclude the proposed testimony of Defendants' experts is pending before the Court. References to Defendants' experts are made only to summarize Defendants' positions and arguments.

reliable evidence supporting their causation theory. In particular, Plaintiffs assert two sub-theories supporting their general causation claim that unprocessed bone tissue stored at room temperature for thirty days or more is capable of transmitting the diseases at issue: (1) lyophilization does not inactivate viruses and is a known method of preserving viruses; and (2) the bone structure protects viruses. (Mem. in Supp. of Pls.' Resp. to Defs.' Mot. for Summ. J. and Pls.' Cross-Mot. for Summ. J. 16-18.) These sub-theories have been discussed in depth in the Court's review of Defendants' motions to exclude the proposed testimonies of certain of Plaintiffs' experts. The Court in this Opinion has excluded portions of the proposed testimony of Drs. Kowalski, Klein, Manzarbeitia, and Parisian to the extent that they proposed to opine regarding the transmission of syphilis, cancer, HIV, HBV, and HCV in bone allografts stored at room temperature for thirty days or more as well as the transmission of prion disease through unprocessed bone allografts. Without Plaintiff's expert evidence, there is no evidence supporting Plaintiffs' theories that lyophilization preserves the viruses at issue in this litigation and that the bone structure protects viruses such that these bone allografts cannot transmit disease after storage at room temperature for thirty days or more.

The Court will first address the causation element for each disease in turn.

Then, the Court will turn to the remaining areas of contention.

i.) Syphilis

Plaintiffs have failed to provide any evidence suggesting that syphilis, a disease caused by a bacteria,[41] can be transmitted by unprocessed bone tissue that has been stored at room temperature for thirty days or more. Although none of Plaintiffs' experts have opined that syphilis may be transmitted in this fashion, Plaintiffs' counsel have cited certain evidence in support of their position. First, Plaintiffs argue generally that bacterial spores are hardier than viruses and that bacterial infections can be transmitted by transplanted tissue for long periods of time. (Mem. in Supp. of Pls.' Resp. to Defs.' Mot. for Summ. J. and Pls.' Cross-Mot. for Summ. J. 32.) However, they have failed to identify any literature that indicates transmission of the bacteria at issue here, the spirochete bacteria, can remain viable under these circumstances. Second, Plaintiffs' counsel cite articles that demonstrates that the *frozen* spirochete bacteria can be preserved in a medium after storage for several years. (Mem. in Supp. of Pls.' Resp. to Defs.' Mot. for Summ. J. and Pls.' Cross-Mot. for Summ. J. 32-33, n. 103.) These studies clearly are not reasonable support for Plaintiffs' causation theory with respect to syphilis without extrapolation from any experts. Third, to the extent that Plaintiffs rely

[41] Syphilis is caused by a spirochete bacteria. (Busch Dep. 27.)

upon guidelines for donor screening as evidence of causation, it is merely speculative. Finally, Plaintiffs' attempt to prove general causation by relying on the factual complaint of one of the plaintiffs in this litigation is clearly the tail wagging the dog. In essence, Plaintiffs have failed to provide evidence, other than counsel's argumentation and attempts to extrapolate causation from tangential or speculative evidence, that syphilis can be transmitted by unprocessed bone tissue that has been stored at room temperature for thirty days or longer.

The Court, therefore, concludes that there is no genuine issue of material fact in dispute, and Plaintiffs have failed to evidence general causation as to syphilis.

ii.) Cancer

Plaintiffs have similarly failed to provide any reliable evidence that cancer can be transmitted in unprocessed bone tissue stored at room temperature for thirty days or more. In support of their theory of general causation with regards to cancer, Plaintiffs direct the Court's attention to one of their experts, Dr. J. Scott Nystrom, who identified problems with Defendants' expert Anna Meadows's opinion that cancer cannot be transmitted from freeze-dried bone at room temperature. (Nystrom Aff. ¶¶3-5, May 31, 2007.) As the non-moving party with the burden of proof at trial, Plaintiffs must put forth some evidence that could

establish general causation at trial. Plaintiffs have failed to do so.

In fact, Defendants point to testimony contrary to Plaintiffs' theory from both their own expert, Dr. Meadows, and Plaintiffs' expert, Dr. Nystrom. Both experts are oncologists. Dr. Meadows opined that cancer cannot be transmitted from freeze-dried bone stored at room temperature for two days or more. (Meadows Aff. 2, Apr. 30, 2007.)[42] Dr. Nystrom generally agreed with Dr. Meadows's statement that "cancer cells are programed genetically to multiply and divide and to make more of themselves . . . but can only do this if they are supplied with the essential nutrients that are available and specialized to suit culture medium or if they're immediately introduced into a living organism where they will be bathed with oxygen and other essential nutrients." (Nystrom Dep. 54.) Furthermore, he testified in response to a question about the viability of cancer cells after thirty days, "Correct. I mean the presumption is for 30 days I would think everything should be dead." (Nystrom Dep. 85.)

As Plaintiffs' expert appears to agree with Defendants' unchallenged expert opinion that cancer cells would be dead within thirty days and Plaintiffs' have not provided any evidence to refute Defendants' theory, the Court finds that there is no genuine issue of material fact in dispute on this issue.

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[42] Plaintiffs' have not moved to exclude the proposed testimony of Dr. Meadows.

iii.) HIV

Defendants assert that there is no genuine issue of material fact that HIV cannot be transmitted by unprocessed bone tissue kept at room temperature for thirty days or more. They advance several theories for this conclusion based upon the opinions of their experts, statements by Plaintiffs' experts, and support from relevant scientific literature for their conclusion that: (1) there have been no scientific literature that has identified a case where HIV has been transmitted by bone tissue stored at room temperature; (2) laboratory studies have demonstrated that HIV cannot effectively be maintained in blood at room temperature, even when additives are used to stabilize and protect the virus; (3) the volume of blood in bone is relatively low, and therefore, the amount of virus in bone is probably less and certainly not more than whole blood; and (4) Defendants' experts and one of Plaintiff's experts Dr. Busch have all rejected the "possibility of HIV transmission by room temperature bone tissue." (Mem. in Supp. of Defs.' Mot. for Summ. J. 15.) In response, Plaintiffs attempt to undermine the Defendants' use of certain medical literature and then proffers the Buck, Crawford, and Uhlenhaut studies to demonstrate that the lyophilization of viruses does not inactivate those viruses.

The Court finds that Plaintiffs have not put forth any reliable evidence

sufficient to meet its burden on a summary judgment motion.[43] Plaintiffs as the non-moving party are entitled to have all inferences from the evidence in their favor. It bears reiterating that this summary judgment standard, however, does not excuse the party who must bear the ultimate burden of proof at trial from setting forth some affirmative evidence to support an essential element of their claims. Defendants in their summary judgment motion need only demonstrate the absence of Plaintiffs' proofs—not that there is some evidence in support of their position. Thus, the Court must examine whether there is any affirmative evidence in support of Plaintiffs' theories of the litigation.

In this case, Plaintiffs have failed to provide any evidence of general causation with respect to the transmission of HIV through the transplantation of unprocessed human cadaveric bone tissue that has been stored at room temperature for thirty or more days. As discussed extensively in the Court's analysis of Defendants' motion to exclude the proposed testimony of certain of Plaintiffs' experts, these studies alone do not directly provide support to Plaintiffs' theory of general causation. With the Court's exclusion of certain opinions of

[43] The Court reiterates that references to Defendants' experts are merely to summarize Defendants' arguments. As Plaintiffs' motion to exclude certain of Defendants' experts is pending before the Court, the Court will not consider Defendants' expert opinions in assessing whether there are any genuine issues of material fact in dispute.

Plaintiffs' experts, Plaintiffs cannot reliably extrapolate the results of these studies so that they are relevant to this litigation. Therefore, the Court is left with no evidence in support of Plaintiffs claim of general causation and must grant Defendants' motion for summary judgment with respect to the transmission of HIV in unprocessed bone tissue stored at room temperature for thirty days or more.

iv.) HBV & HCV

Defendants' challenge of Plaintiffs' proofs regarding the transmission of HBV or HCV in unprocessed bone tissue stored for over thirty days is similar to that of HIV. They contend that HBV and HCV cannot be transmitted by such bone based upon the opinions of their experts as well as scientific literature for their conclusion that: (1) there is no scientific literature that has identified a case where HBV or HCV has been transmitted by bone tissue stored at room temperature, and the Tugwell case study supports this conclusion; (2) laboratory studies have demonstrated that HBV or HCV cannot remain infectious at room temperature; (3) the number of alleged HCV plaintiffs is consistent with the prevalence of HCV in the general population; and (4) Defendants' experts have all concluded that unprocessed bone tissue kept at room temperature for thirty days or more cannot transmit HBV or HCV. (Mem. in Supp. of Defs.' Mot. for Summ. J. 15-18.)

Plaintiffs attempt to undermine the Defendants' use of the Tugwell Study by proffering the opinions of its experts, Drs. Manzarbeitia and Parisian, as well as the Buck, Crawford, and Uhlenhaut studies to demonstrate that the lyophilization of viruses does not inactivate those viruses. Furthermore, Plaintiffs assert that the plaintiffs who claim hepatitis infection by bone transplants in this litigation represent 5% of the filed cases and is higher than what is expected in the general population.

The Court finds that Plaintiffs have again failed to provide any evidence of general causation with respect to the transmission of HBV or HCV through the transplantation of unprocessed human cadaveric bone tissue that has been stored at room temperature for thirty or more days. As discussed extensively in the Court's analysis of Defendants' motion to exclude the proposed testimony of certain of Plaintiffs' experts, these studies alone do not directly provide support to Plaintiffs' theory of general causation. With the Court's exclusion of certain opinions of Plaintiffs' experts, Plaintiffs cannot reliably extrapolate the results of these studies so that they are relevant to this litigation. Furthermore, to the extent that Plaintiffs attempt to suggest an epidemiological theory of causation from those plaintiffs in this litigation who have alleged disease transmission, such a circular proof of

general causation is unwarranted.[44] Therefore, the Court is left with no evidence in support of Plaintiffs claim of general causation and must grant Defendants' motion for summary judgment with respect to the transmission of HBV and HCV in unprocessed bone stored at room temperature for thirty days or more.

4. Transmission of Prion Diseases

Defendants argue that the risk, if any, of the transmission of prions through bone tissue, at this point in time, is purely theoretical and merely speculative. (Mem. in Supp. of Defs.' Mot. for Summ. J. 23.) Plaintiffs argue that bone is a viable agent capable of transmitting prion diseases. In support, they refer to experimental studies involving animals to demonstrate their theory that prions can adhere to the surface of bone and thereby transmit disease. Plaintiffs also proffer the testimony of Dr. John Conomy. Although he has acknowledged that bone used in allograft procedures "would bear a substantial risk of transmitting disease" (Conomy Dep. 161), Dr. Conomy admitted that he was unable to opine about this risk without making many assumptions. (Conomy Dep. 161.)

His opinion regarding the risk of transmitting prions through bone allograft tissue was speculative, and when asked whether he could state his conclusion with

[44] Plaintiffs have not presented any expert analysis in this litigation to suggest such a conclusion.

a more-probable-than-not standard, he answered:

> "I'd have to make a lot of assumptions along the way. If I made a pile of assumptions about the burden of disease and the amount of *bone marrow* and then the kinds of cells and whether there was contamination by some nervous system source, there are lots of variable in it. But if they were all piled up, then the probability would be more than not. If, however, none of these things pertained, it would not be more than not. I wish I could, you know give you a flat-out answer, but there's no scientific or clinical evidence for that. So what is not known from the scientific laboratory or from the clinic can't be, you know, stated dispositively by a court."

(Conomy Dep. 161-62) (emphasis added.) Dr. Conomy's answer demonstrated the lack of certainty to which he was able to form an opinion regarding this issue. The lack of literature and knowledge of this disease is consistent with the opinion of Defendants' expert Barnaby May, Ph.D., who opined that although there is a theoretical risk of prion transmission through bone tissue, it is pure speculation at this time within the field. (May Dep. 67.)[45] Therefore, the Court cannot conclude from these statements that there is sufficient evidence of general causation on the issue of prion transmission through bone transplants.[46] Thus, Plaintiffs have not created a genuine issue

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[45] Plaintiffs have not challenged Dr. May's proposed testimony under Fed. R. Evid. 702 or *Daubert*.

[46] The Court recognizes that Defendants have not challenged Dr. Conomy's testimony under *Daubert*. The Court finds, rather, that Dr. Conomy's proposed testimony is so vague and speculative that it cannot form the basis for any factual dispute.

of material fact regarding the absence of general causation with regards to the transmission of prions.

5. Bone Paste

Defendants also seek summary judgment on the issue of bone paste. They argue that bone paste cannot transmit disease regardless of the temperature of the bone paste or the amount of time that bone paste has been stored at room temperature. In support of their argument, Defendants rely upon the fact that there are no reports documenting the transmission of the disease at issue by bone paste. Plaintiffs contend that the lack of any reported cases of disease transmission by bone paste is a red herring since there is no literature at all assessing the ability of bone paste to transmit disease.

On the issue of disease transmittal, the Court finds no reason to differentiate bone paste from other bone allografts at issue in this litigation at this time.[47] Therefore, the Court will not grant Defendants' motion for summary judgment on the ability of bone paste, regardless of the temperature and duration of storage, to transmit disease.

6. Incubation Period of HIV, HBV, HCV, and Syphilis

[47] Although bone paste and allograft bone tissue are subject to different processing steps, it is undisputed that both processes involve drying through a method like lyophilization and storage at room temperature. (Mem. in Supp. of Defs.' Mot. for Summ. J. 5, n. 13, 7.)

Defendants have moved for summary judgment on the issue of the incubation periods, the period between exposure to an infectious agent and detection of infection, for HIV,[48] HBV, HCV, and syphilis. Defendants argue that the incubation periods are less than six months. Defendants also cite to the FDA and CDC recommendations advising testing for recipients up to six months after transplantation of BTS-recovered bone tissue. (Mem. in Supp. of Defs.' Mot. for Summ. J. 36.) Therefore, they argue that testing negative for these diseases after six months is conclusive as to the existence or non-existence of an infection and that no further testing is required. Plaintiffs assert that the incubation period for HIV, HBV, and HCV is longer than six months.[49] The Court disagrees with Plaintiffs.

i.) HIV

Defendants contend that the leading authoritative sources[50] as well as

[48] There is some confusion over whether Plaintiffs are contesting the incubation period of HIV beyond six months. In their opposition to Defendants' Motion to Exclude, Plaintiffs state that the experts agreed that the incubation period for HIV is six months. (Pls.' Mem. in Opp. to Defs.' Mot. to Exclude 2.) In oral arguments, however, Plaintiffs' counsel stated that they did not concede the incubation period for HIV. (Hr'g Tr. 10, Sept. 4, 2008.)

[49] Plaintiffs conceded that the incubation period for syphilis infection is less than six months. (Hr'g Tr. 10, Sept. 4, 2008 .)

[50] These sources include the CDC, U.S. Department of Health and Human Services, Iowa Department of Public Health. (Mem. in Supp. of Defs.' Mot. for Summ. J. 32-33.)

Plaintiffs' own expert Dr. Busch[51] support a finding that the incubation period for HIV is less than six months with the vast majority of individuals with detectable antibodies within three months.[52] Plaintiffs merely challenge Defendants' assertions by suggesting that the CDC information is untimely and fails to account for the FDA's approval of NAT testing. Plaintiffs' argument is puzzling to the Court since the FDA's press release with respect to its approval of NAT testing is not contrary to the six-month incubation theory proposed by Defendants for HIV and reinforces the idea that with certain testing, the incubation period is much shorter. (DePalma Cert. Ex. OO.) Thus, with the Court's exclusion of Plaintiffs' expert Dr. Klein and the presentation of no contrary evidence by Plaintiffs, the Court finds that there is no material issue of fact in dispute regarding the six-month incubation period for HIV, and the Court will grant summary judgment to Defendants on this issue.

ii.) HBV & HCV

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[51] Dr. Busch stated that the standard time for HIV would be between ten and twenty days, "but outliers as far as 6 months." (Busch Dep. 81.)

[52] For the purposes of fully summarizing Defendants' position, the Court notes Defendants' assertion that their experts conclude that the incubation period for HIV is less than six months: Dr. Kuritzkes (three to four weeks, six months at most); Dr. Jarvis (fifteen days); Dr. Richman (one week to one month); and, Dr. Rutala (one to three months). (Mem. in Supp. of Defs.' Mot. for Summ. J 34.) As the Court has not addressed Plaintiffs' motion to exclude these experts, the Court does not rely upon the testimony of Defendants' experts in assessing the summary judgment motion.

Defendants argue that the leading authoritative sources[53] conclude that the incubation period for HBV and HCV is less than six months, and that Plaintiffs have provided no evidence to the contrary.[54] The Court agrees.

With the Court's exclusion of Drs. Klein and Manzarbeitia's opinions regarding the incubation period for HBV and HCV, Plaintiffs have provided no admissible evidence to support their contention that the incubation period for HBV or HCV is greater than six months within the general population and that testing beyond six months is required to rule out infection. First, Plaintiffs' reliance upon a 2007 chimpanzee study,[55] finding prolonged incubation periods with low level inoculations of HBV, is insufficient evidence to create a genuine

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[53] These sources include the CDC as well as other state and international health departments. (Mem. in Supp. of Defs.' Mot. for Summ. J. 25, 29.)

[54] For the purposes of fully summarizing Defendants' position, the Court notes Defendants' assertion that their experts universally opined that the incubation period for HCV was less than six months: Dr. Jarvis (fifty-nine days); Dr. Rutala (six to nine weeks with a range of two to twenty-six weeks); Dr. Richman (within two months); Dr. Kainer (six to nine weeks); and, Dr. Koziel (six months maximum). (Mem. in Supp. of Defs.' Mot. for Summ. J. 26.) With regards to HBV, Defendants similarly assert that their experts universally opined that the incubation period was less than six months: Dr. Jarvis (80.5 days); Dr. Rutala (sixty to ninety days with a range of forty- five to 180 days); Dr. Richman (several weeks, one to two months); Dr. Koziel (six months); and Dr. Kainer (sixty to ninety days, range forty-five to 180 days). (Mem. in Supp. of Defs.' Mot. for Summ. J. 29.) Again, as the Court has not addressed Plaintiffs' motion to exclude these experts, the Court does not rely upon the testimony of Defendants' experts in assessing the summary judgment motion.

[55] The study entitled, "Minimum Infectious Dose of Hepatitis B Virus in Chimpanzees and Difference in the Dynamics of Viremia between Genotype A and C," by Yutaka Komiya, et al. was published in the journal *Transfusion*.

dispute of material fact as the authors expressly stated that the results of the study could not reliably be extrapolated into the human context. (Mem. in Supp. of Pls.' Resp. to Defs.' Mot. for Summ. J. and Pls.' Cross-Mot. for Summ. J. 43-44; DePalma Cert. Ex. LL 15, Nov. 21, 2007.) Second, Dr. Busch, whose opinion was not challenged under *Daubert* by Defendants, opined that the traditional serological antibody testing would be adequate to detect HBV and HCV infection within six months except in "rare, rare cases" with "silent infections" where a defective HCV was the cause of infection or in occult infections, or in low-level HBV inocula where the recipients were temporarily immunocompromised. (Busch Dep. 83-84, 86-87; Mem. in Supp. of Pls.' Resp. to Defs.' Mot. for Summ. J. and Pls.' Cross-Mot. for Summ. J. 42-43.) Third, consistent with the general consensus in the relevant medical and scientific community, Plaintiffs' citation to the Beld, Prieto, and Dickson studies, discussed at length in the Court's analysis of Defendants' motion to exclude, identifies only exceptional outlier liver transplant patients and illicit drug users. The results of these extremely limited studies cannot, without extrapolation, create a genuine issue of material fact in dispute for the general population. Finally, even in these exceptional cases or groups with high risk exposure, Dr. Busch further opined that "if [the recommendation] includes the combination of nucleic acid and serologic testing, I think six months

is appropriate." (Busch Dep. 86.) Therefore, the Court is without sufficient evidence to conclude that there is a material issue of fact in dispute regarding the six-month incubation period for HBV and HCV among this group of plaintiffs.

With regards to Plaintiffs' argument that nucleic acid tests (NAT) as well as the traditional antibody tests are required to rule out infection. The Court is similarly unpersuaded. As discussed above, the traditional serological antibody test can detect HBV and HCV infection for the general population within six months. For those limited sub-populations where traditional serological antibody testing may not detect HBV and HCV infection within six months, detection of infection may be possible with NAT testing within six months. The determination of whether a NAT test, as opposed to a traditional serological antibody test, is appropriate for a plaintiff due to his or her membership in one of these limited groups or his or her medical history is best left in the hands of Plaintiff's treating physician, not the Court. Therefore, the Court will not require NAT testing to rule out HBV and HCV infections.

7. Appropriateness of Summary Judgment

Plaintiffs in their opposition to Defendants' motion for summary judgment contest the granting of summary judgment as: (1) this is the "first" experiment of massive unscreened donors, and therefore, there is no literature to support their

theories; (2) the questions posed by the Court have not been directly explored by the medical and scientific community; and (3) there has been limited discovery in this case. Although the Court is mindful of the challenges confronting Plaintiffs' ability to construct this type of case, the entry of partial summary judgment cannot be avoided.

Multidistrict litigation courts are often confronted with evaluating limited or evolving scientific and medical theories and evidence. The absence of definitive scientific or medical knowledge is unfortunately a reality in some cases. Nevertheless, district courts are charged with the role of gatekeeper and can only allow presently reliable evidence. As other courts have recognized, the Rules of Evidence may, on occasion, prevent the jury from learning about promising or potential clinically relevant information. *See In re Reuzulin Products Liability Litigation*, 369 F. Supp. 2d 398, 438 (S.D.N.Y. 2005). The Rules of Evidence, however, cannot be disregarded even if at a future date, medical and scientific literature proves the contrary. As Judge Richard Posner put, "the courtroom is not the place for scientific guesswork, even of the inspired sort. Law lags science; it does not lead it." *Rosen v. Ciba-Geigy Corp*., 78 F.3d 316, 319 (7th Cir. 1996).

The causation questions posed by the Court with input from the parties were intended to guide the parties to common issues of fact and law. The parties

ultimately shaped the course of their challenges and proofs. As these questions deal with issues of general causation on the science of transmission, extensive party discovery, aside from expert discovery, was unnecessary. Thus, summary judgment on the issues before the Court is appropriate.

8. Conclusion

In summary, Plaintiffs have failed to provide any reliable evidence to support their claims of general causation with respect to the transmission of HIV, HBV, HCV, cancer, and syphilis through unprocessed human bone tissue that has been stored at room temperature for thirty days or more before transplantation into an individual and the transmission of prion disease through human cadaveric bone tissue. Furthermore, Plaintiffs have failed to put forth any reliable evidence to support their claims that those plaintiffs who have tested negative for HIV, HBV, HCV, and syphilis after six months from exposure to potentially infectious bone tissue are capable of developing these diseases from such bone tissue. Nor does the record support any genuine dispute of material fact as to the issues of transmission and incubation. Therefore, the Court will grant Defendants' summary judgment motion as to these specific issues. Beyond these limited issues of general causation, the Court will reserve on the implications of the grant of partial summary judgment.

C. Plaintiffs' Motion for Summary Judgment and Motion to Exclude Certain of Defendants' Proposed Expert Testimony

Plaintiffs request summary judgment on the issues of whether: (1) the diseases at issue in this litigation can be transmitted to those who received frozen and fresh-frozen bone allografts; and (2) these diseases can also be transmitted to those who received lyophilized allografts less than thirty days from recovery of the tissue. Defendants oppose the motion, and concede only that: (1) frozen bone tissue, which is not stored at room temperature, may transmit certain diseases; and (2) unprocessed bone tissue stored at room temperature for a matter of hours or days may transmit certain diseases. The Court reserves on this motion as well as on Plaintiffs' motion to exclude certain of Defendants' experts pursuant to Fed. R. Evid. 702 and *Daubert*.

IV. CONCLUSION

For the foregoing reasons, Defendants' motion for summary judgment and motion to exclude are granted in part. Plaintiffs' cross-motion for summary judgment and motion to exclude are reserved. An appropriate Order accompanies this Opinion.

s/William J. Martini
William J. Martini, U.S.D.J.

Dated: October 22, 2008