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RISK AND REWARD IN STEM CELL PRODUCTS: A NEW MODEL FOR STEM CELL PRODUCT LIABILITY

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ABSTRACT

Stem cell products have the potential to give patients access to treatments and cures for diseases and conditions that are currently beyond the scope of modern medicine. There are not yet many stem cell products on the market in the United States, but soon there will be. It therefore makes sense to explore how we should deal with policy issues concerning these products now.

This Article examines the problem of how best to handle legal liability for any harm that stem cell products cause. At present, a complex patchwork of federal and state statutes and legal precedents determines whether makers of drugs, biologics, medical devices and combination products are liable for defects. None of these legal materials specifically addresses stem cell products. Because stem cell product development is in its infancy, and because the risks of stem cell products are largely unknown, it is critical that the correct legal regime be in force. Too much legal liability could inhibit research into stem cell product development. Not enough legal liability could unnecessarily harm patients and hinder the use of stem cell products.

This Article crafts a proposal for what the legal rules ought to be for stem cell products to best benefit all parties involved. Far from indulging in standard neoclassical economic analysis, I employ work on bounded rationality, game theory, and other developments to come up with a proposal that has a better chance of working in the real world and with actual, non-maximizing individuals who have inadequate information. In brief, the proposal is a qualified system of strict liability for stem cell products in which

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patients and manufacturers contribute on a per-product basis to a compensation fund and the federal government acts as an insurer of last resort. Unlike most writing in this area, the liability proposal takes the ethics of risk imposition seriously.

I. INTRODUCTION

Stem cell products could potentially cure and treat diseases and conditions that are beyond the current reach of modern medicine. Because stem cell products carry such promise, it is important to introduce them to the public in a

way that will maximize their utility while minimizing the damage they could cause. A proper grasp of stem cell products reveals that their risks and rewards differ markedly from the risks and rewards associated with drugs, medical devices, other biological products, and so-called combination products. These differences require a new specialized regime of product liability in the case of products emerging from stem cell research and development.

Although one can only surmise the specific risks stem cell products may pose, it would be foolish to forestall discussing their impact on our liability regime until they reach the market. Even then, the risks associated with their use will likely remain undetermined, with product development characterized by trial and error. Upon the initial use of stem cell products, there may be unanticipated side effects and injuries to a portion of the patient population, just as there have been with other new products and therapies. Without a proper product liability regime in place before these products are in widespread use, several major setbacks to their continued development may result.

For instance, if injured patients are unable to recover for injuries attributable to defective products, then that could discourage other prospective patients from using related stem cell products. Moreover, if there is little risk of legal liability, manufacturers of stem cell products may be more likely to introduce unsafe products to the market. Their introduction would raise the number of patient injuries and cause a decline in the market for better stem cell products. Conversely, if patients were able to recover damage awards too easily, manufacturers could be discouraged from entering the stem cell product market in the first place.

Grappling with these potential contingencies before they occur is a type of "upstream precaution."[1] The need to contain these problems after they have spread, with "downstream precautions," may be avoided if an effective, well-designed regime of stem cell product liability is put in place now.[2] Further, downstream precautions are often incapable of rectifying harm that could have been prevented with proper upstream precautions. For this reason, it is more fruitful to devise a liability scheme before new stem cell products begin to enter the market.

This Article thus addresses how best to handle legal liability for any harm that stem cell products might cause. Solving this problem is quite difficult despite the long history of product liability law. The basic answer may seem

[1] I am indebted to Carl F. Cranor, Protecting Early Warners and Late Victims in a Precautionary World (Oct. 25, 2011) (unpublished manuscript) (on file with author), for the vocabulary of upstream and downstream precautions, which I use a bit differently from him.

[2] *Id.*

obvious: Who bears financial responsibility for harm caused by stem cell products should be governed by product liability law, which is part of the law of tort. Under it, makers of defective stem cell products are liable for three varieties of legal fault: (1) intentional wrongdoing, which is rare, (2) recklessness, which is unusual, and (3) negligence, which is fairly common. However, product liability law does not end there. In certain cases producers and manufacturers can be liable without regard to fault, namely strict liability.[3]

Moreover, a patchwork of federal and state statutes and legal precedents determines whether makers of drugs, medical devices, and various biologics are strictly liable for harm caused by their products. Depending on whether strict liability or negligence law is applied in a particular case, the incentives for introducing products to the market can change drastically. In the case of stem cell products, it is especially difficult to determine what the relevant existing legal rules are and how they will apply, because right now there are very few stem cell products and no rules that clearly govern them. Furthermore, even if existing legal rules can be elucidated, a deeper issue is waiting in the wings: what *should* the legal rules be?

In an attempt to answer this question, I propose a modified strict liability regime for stem cell products that are defective in design or manufacture or have inadequate warnings. The analysis I use to devise this new regime takes thoughtful consideration of each party involved in the use of a stem cell product. Those parties include designers, manufacturers, physicians, and patients. I hope that it will not be rash to claim that my analysis of risk and reward goes beyond the usual neoclassical economic treatments of product liability. At the end the reader will have to judge whether I have made good on this claim.

The Article proceeds as follows: Part II sets the stage for my arguments by briefly introducing stem cell products and the ways in which they might be classified. Part III sets out the basic principles behind product liability for drugs and medical devices, followed by an in-depth analysis of the likely weaknesses associated with applying current product liability law to stem cell products. Part IV addresses the economic concerns of a product liability

[3] Negligence requires a breach of a duty of care, whereas strict liability requires no such breach. *Greenman v. Yuba Power Products, Inc.*, 377 P.2d 897 (Cal. 1963), was the first case in the United States to recognize strict product liability in tort. Such liability requires that the product be defective in manufacture or design or that adequate instructions or warnings be absent. RESTATEMENT (THIRD) OF TORTS: PRODUCTS LIABILITY § 2 (1998) [hereinafter R3D PRODUCTS LIABILITY]. For discussion of this work with regard to drugs, see Lars Noah, *This is Your Products Liability Restatement on Drugs*, 74 BROOK. L. REV. 839 (2009).

scheme with a discussion of neoclassical economics, bounded rationality, game theory, the underpinnings of welfare economics, and other developments. Drawing upon the conclusions of Part IV, Part V deploys a novel liability regime for stem cell products. Here I suggest a product liability regime that has a better chance than neoclassical economic regimes of working in the real world, with actual, non-maximizing individuals who have inadequate information. Using these developments, I propose a qualified system of strict liability for stem cell products in which patients and manufacturers contribute on a per-product basis to a compensation fund and the federal government acts as an insurer of last resort. Part VI concludes.

II. STEM CELL PRODUCTS AND THEIR CLASSIFICATION

A. What Is a Stem Cell Product?

The reader has every right to know what stem cell products are and what manner of stem cell products might be on the market. Otherwise, my arguments will lack concreteness. To begin, a stem cell is distinctive because it has not "differentiated" into a fully specialized cell (e.g., skin cell, brain cell, or blood cell).[4] Once a cell becomes specialized, its particular function is "fixed" and ordinarily cannot change.[5] Human embryonic stem cells ("hESCs") are "pluripotent," which denotes that they can differentiate into any type of human cell.[6] Some human adult stem cells are "multipotent," which means that they may differentiate into a number of closely related human cells.[7]

The term *stem cell product* covers many different items. Among them are primary human embryonic stem cells ("hESCs"), human embryonic stem cell ("hESC") lines, more committed cells derived from them (e.g., neural precursors), fully differentiated cells coming from hESCs or hESC lines (e.g., neurons, cardiomyocytes, and pancreatic islet cells), and patient-specific smooth muscle tissue or bladders created by somatic cell nuclear transfer ("SCNT"). Hematopoietic stem cells are blood-forming cells, which come

[4] RUSSELL KOROBKIN, STEM CELL CENTURY: LAW AND POLICY FOR A BREAKTHROUGH TECHNOLOGY 7 (2007).

[5] *Id.* There are some exceptions involving dedifferentiation and induced pluripotent stem cells, but these need not detain us here. On the latter, see *infra* note 20.

[6] KOROBKIN, *supra* note 4, at 8.

[7] *Id.* at 10. For an account of the full range of stem cells and some difficulties with the concept of stemness, see Yan Leychkis, Stephen R. Munzer & Jessica L. Richardson, *What is Stemness?*, 40 STUD. IN HIST. & PHIL. OF BIOLOGY & BIOMEDICAL SCI. 312 (2009).

from bone marrow and umbilical cord blood. They have been used for some while to treat various hematologic malignancies and other blood-related diseases.[8] Some might say that hematopoietic stem cells are not so much products as treatments. Be that as it may, there are at present very few non-hematopoietic stem cell products on the market. The FDA has characterized stem cell therapies and treatments as products.[9]

Because stem cells can be enlisted to create a wide variety of products, the products will likely be used for a highly diverse range of diseases and conditions. Some promising medical targets and their corresponding stem cell products follow. Type 1 Diabetes might be put into remission by injecting insulin-producing cells derived from hESCs,[10] and eventually an artificial pancreas crafted in part from these cells might replace a patient's defective pancreas.[11] Heart disease treated with heart muscle cells (cardiomyocytes) derived from hESCs could serve as a basis for cardiac-safety pharmacology assays and the discovery of new cardiac drug targets.[12] Moreover, cardiomyoctyes themselves could serve as replacement muscle tissue for heart cells destroyed by a myocardial infarction.[13] Relatedly, it may be possible to

[8] Stephen R. Munzer, *The Special Case of Property Rights in Umbilical Cord Blood for Transplantation*, 51 RUTGERS L. REV. 493, 500-01 (1999). I made some minor adjustments in my position in response to criticisms offered by Donna Dickenson, *An Uneasy Case against Stephen Munzer: Umbilical Cord Blood and Property in the Body*, 8 AM. PHIL. ASS'N NEWSLETTER ON PHIL. & LAW, no. 2, Spring 2009, at 11. *See* Stephen R. Munzer, *Moral, Political, and Legal Thinking: Property and Bioethics,* 8 AM. PHIL. ASS'N NEWLETTER ON PHIL. & LAW, no. 2, Spring 2009, at 16, 21-24 (replying to Dickenson).

[9] 21 C.F.R. §§ 1270, 1271 (2011); *Vaccines, Blood & Biologics: Tissue and Tissue Product Questions and Answers*, U.S. FOOD & DRUG ADMIN., http://www.fda.gov/BiologicsBloodVaccines/TissueTissueProducts/QuestionsaboutTissues/ucm101559.htm (last visited Oct. 1, 2011); *see also* Donald W. Fink, Jr., *FDA Regulation of Stem Cell-Based Products,* 324 SCIENCE 1662, 1662 (2009).

[10] *Clinical Application: Diabetes and Insulin*, VIACYTE, http://www.viacyte.com/trials/index.html (last visited Oct. 1, 2011); *cf.* Andrew Pollack, *Stem Cell Therapy Controls Diabetes in Mice,* N.Y. TIMES, Feb. 21, 2008, at A16 (describing a similar advance in mice).

[11] M. J. Friedrich, *Artificial Pancreas May Soon Be a Reality*, 301 JAMA 1525 (2009). *See generally* JUAN DOMÍNGUEZ-BENDALA, PANCREATIC STEM CELLS (Kursad Turksen ed., 2009).

[12] *Cardiomyocytes: hES-CMC™ - Cardiomyocyte Clusters*, CELLARTIS, http://www.cellartis.com/products/differentiated-cells/cardiomyocytes (last visited Oct. 1, 2011).

[13] Carolyn Y. Johnson, *Harvard Discovery Gives New Tools for Drug Development,*

use biodegradable scaffolds seeded with cardiomyocytes produced from human stem cells "to treat congenital heart defects in the young or chronic heart disease in the elderly."[14] Spinal cord injuries may be treated with central nervous system cells derived from hESCs, such as oligodendroglial precursor cells, which could replace similar cells destroyed or compromised by physical trauma.[15] Stem cells may also be differentiated into artificial organs. Because most internal organs have an enveloping capsule of tissue, work on weaving hESC cells into polymer threads holds promise for encapsulation as well as for creating tissues inside organs.[16] Trachea surgery may be treated with a transplant: after harvesting a trachea from a donor and stripping off all donor cells except the cartilage cells, or chondrocytes, it is possible to use induced pluripotent stem ("iPS") cells or even hematopoietic stem cells from the patient to line the donor trachea and transplant it into the patient.[17] For neurodegenerative disorders, it may be possible to use neural precursors derived from stem cells to produce various kinds of brain cells to treat Alzheimer's and Parkinson's diseases.[18] And in the case of eye diseases, stem

BOSTON GLOBE, July 2, 2009, at 7 (describing the use of hESCs to develop a "master" heart cell which can differentiate into heart cells of various sorts for use in drug development and regenerative medicine).

[14] Steven Connor, *Stem-Cell Technique May End Need for Heart Donors,* THE INDEPENDENT, Nov. 3, 2008, at 8; *cf.* George C. Engelmayr et al., *Accordion-Like Honeycombs for Tissue Engineering of Cardiac Anisotropy*, 7 NATURE MATERIALS 1003, 1003 (2008).

[15] Wise Young, *Geron's Oligodendroglial Precursor Cell Therapy Trial*, WISE YOUNG @CARECURE (Jan. 27, 2009, 1:31 PM), http://wiseyoung.wordpress.com/2009/01/27/geron.

[16] Anil Abeyewickreme et al., *Bio-Electrospraying Embryonic Stem Cells: Interrogating Cellular Viability and Pluripotency,* 1 INTEGRATIVE BIOL. 260 (2009) (using murine ES cells); Colin Barras, *Stem Cell "Fabrics" Promise Universal Tissue,* NEW SCIENTIST (Feb. 26, 2009, 3:10 PM), http://www.newscientist.com/article/dn16670-stem-cell-fabrics-promise-universal-tissue.html (offering a nontechnical explanation of the process).

[17] Alan Cowell & Denise Grady, *Europeans Announce An Advance In Surgery,* N.Y. TIMES, Nov. 20, 2008, at A8 (describing success of trachea surgery that uses patient's stem cells); Paolo Macchiarini et al., *Clinical Transplantation of a Tissue-Engineered Airway,* 372 LANCET 2023 (2008) (reporting that the patient had no anti-donor antibodies and was not on immunosuppressive drugs four months after the procedure).

[18] *See, e.g.*, Martine Geraerts et al., *Concise Review: Therapeutic Strategies for Parkinson Disease Based on the Modulation of Adult Neurogenesis*, 25 STEM CELLS 263 (2007); Olle Lindvall & Zaal Kokaia, *Stem Cells for the Treatment of Neurological Disorders*, 441 NATURE 1094 (2006).

cell derived retinal cells could treat some sorts of blindness.[19] The treatment of these and other diseases and conditions depends to some extent on the safe and effective use of pluripotent stem cells that are induced from a patient's own cells rather than hESCs.[20] How soon these and other possible advances will materialize as widely used treatments is not known.

B. How Will Stem Cell Products be Classified?

Determining how stem cell products are likely to be classified by the FDA is a helpful first step toward applying the correct product liability measures to them. For example, if a stem cell product is most similar to a drug in terms of its mode of activity, formulation, and risk profile, then it should be classified as a drug product. Then, the most analogically relevant legal and analytical precedents should come from cases involving drugs. From these precedents, one could elucidate the incentives given to researchers, manufacturers, physicians, and patients. Finally, based on the legal and economic effects of precedents, one might in principle craft a liability system.

In fact, however, drugs are not similar enough to stem cell products to form a good liability model. We need to cast our net more widely. At present, there are four categories under which the FDA could place stem cell products: (1) drugs, (2) biologics, (3) devices, and (4) combination products. The FDA is unlikely to put *all* stem cell products into any *one* of these four categories. For example, under the Federal Food, Drug and Cosmetic Act ("FFDCA"), very few stem cell products are apt to be classified as a drug or a device.[21]

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[19] *See, e.g.,* Sarah-Kate Templeton, *Blind to be cured with stem cells,* TIMES (London), Apr. 19, 2009, http://www.timesonline.co.uk/tol/news/uk/health/article6122757.ece. (reporting that ESC-derived eye cells placed on an artificial membrane and inserted in the back of the retina were successful in rats with a disease similar to age-related macular degeneration in humans) [hereinafter cited as *Stem Cells/Macular Degeneration*].

[20] On the prospects for induced pluripotent stem cells, see, e.g., Monya Baker, *Fast and Furious,* 458 NATURE 962 (2009) (noting the surge in interest in iPSCs); Shin-ichi Nishikawa et al., *The Promise of Human Induced Pluripotent Stem Cells for Research and Therapy,* 9 NATURE REVS. MOLECULAR & CELL BIOLOGY 725 (2008). *See also* Mark H. Chin et al., *Induced Pluripotent Stem Cells and Embryonic Stem Cells Are Distinguished by Gene Expression Signatures,* 5 CELL STEM CELL 111 (2009) (explaining that ESCs and iPSCs appear to have different gene expression signatures, although the significance of this finding is unclear); Elie Dolgin, *Gene Flaw Found in Induced Stem Cells*, 464 NATURE 663 (2010) (reporting that in a recent study certain iPSCs had different gene activity from genetically identical ESCs in mice; using human iPSCs rather than hESCs may obviate some moral debates but create others).

[21] 21 U.S.C. § 321(g)(1) (2006) states:

Although the statutory definition of a "drug" might seem to cover some stem cell products, the FDA rarely uses that category for living cells or tissues that have continuing biological action. However, some cells derived from hESCs might generate proteins in large quantities — think of the immune interferon and other proteins produced by the cells from John Moore's body[22] — and these proteins might be classified as drugs. Further, physicians may use a "device" to *deliver* stem cell products to the right place in a patient's body, but the products themselves are not devices.

Most stem cell products will likely be categorized as "biological products," also known as "biologics."[23] The analogy to vaccines is instructive, because,

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> The term "drug" means (A) articles recognized in the official United States Pharmacopoeia, official Homeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clauses (A), (B), or (C).

A paragraph later, 21 U.S.C. § 321(h) (2006) provides:

> The term "device" (except when used in paragraph (n) of this section and in sections 331(i), 343(f), 352(c), and 362(c) of this title) means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is—
>
> (1) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,
>
> (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
>
> (3) intended to affect the structure or any function of the body of man or other animals and
>
> which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

[22] Moore v. Regents of the Univ. of Calif., 793 P.2d 479, 481 (Cal. 1990).

[23] The Public Health Service Act ("PHSA"), *codified as amended at* 42 U.S.C.A. § 262(i) (2011), states:

> In this section, the term "biological product" means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a

like vaccines, a potential therapeutic use for some stem cell products is the reconstitution or strengthening of a patient's immune system. The parallel to whole blood and blood component biological products is also instructive, for hematopoietic stem cells from umbilical cord blood plainly qualify as blood components. The instructiveness is limited, however, because there are many other classes of biologics, such as antitoxins and therapeutic serums, which can prevent, treat, or cure human diseases and conditions.

Many other stem cell products will probably fall in the category of "combination product"—specifically, a combination of a biologic and a device. An FDA regulation defines this term in part as a "product comprised of two or more regulated components, i.e. drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity."[24] Typical examples of combination products are glucose monitor/insulin pump systems, transdermal patches that allow drugs to enter the body slowly through the skin, and cardiac stents that disseminate an antibiotic into the surrounding site and the blood to reduce the risk of infection.[25]

Using stem cells and their derivatives therapeutically also generally requires delivery to an appropriate area of the body. In turn, delivery often requires the use of a device that yields another form of combination product. For instance, some treatments for heart conditions might administer hematopoietic stem cells through catheters into the coronary arteries, or into the myocardium, during a coronary artery bypass graft. Another example is the possibility of having a scaffold seeded with autologous stem cells for organ transplantation. This product would have the shape of the target organ and the autologous cells would allow the product to function, for instance, as a natural human bladder without rejection.[26] Yet another example is the use of a biodegradable scaffold seeded with heart-muscle cells to correct congenital defects and chronic heart

disease or condition of human beings.

With a minor exception, the FFDCA applies to biological products regulated by the PHSA. *See* 42 U.S.C. § 262(j) (2006).

[24] 21 C.F.R. § 3.2(e)(1) (2005). Other items falling under the heading of combination products include separate products that are packaged together or intended to be used together. *See* 21 C.F.R. §§ 3.2(e)(2)-(4) (2005).

[25] For these and other illustrations, see *Examples of Combination Product Approvals*, FDA (July 15, 2010), http://www.fda.gov/CombinationProducts/AboutCombinationProducts/default.htm.

[26] *See* Definition of Primary Mode of Action of a Combination Product, 21 C.F.R. § 3.2(m) (2010).

disease.[27] A further example is employing an artificial membrane, currently being developed by Pfizer, onto which ESC-derived eye cells are placed to treat macular degeneration.[28] These illustrations provide but a small window into possible combination products involving stem cell products.

Because stem cell products, depending on their exact characteristics, might be classified under existing law as biologics, combination products, or, less plausibly, as drugs or devices, one should be alert to the manipulability of this classificatory scheme and special difficulties with some of the pigeonholes. For a start, stem cell products encounter challenges that most non-cellular biologics, such as toxins and antitoxins, do not. Most non-cellular biologics are sterilizable and typically used within thirty days. In contrast, many stem cell products are likely to be cryopreserved for some time, which raises concerns about their stability and requires safeguards for the pre-freeze and post-thaw preservation of the products.[29] Also, many stem cell products, unlike most non-cellular biologics, are unsterilizable, can support the growth of pathogens, and might be placed in sensitive sites such as the central nervous system.[30] Moreover, the FDA center that deals with cellular, tissue, and gene therapies will be alert to parallels between gene therapy and the therapeutic use of stem cell products: unsterilizability, uncertain purity, possible source of pathogens, and risks created by the ongoing biological activity of the new genetic material or cells.[31]

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[27] *See* Connor, *supra* note 14.

[28] *See Stem Cells/Macular Degeneration, supra* note 19.

[29] *See*, *e.g.*, CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION, GUIDANCE FOR REVIEWERS: INSTRUCTIONS AND TEMPLATE FOR CHEMISTRY, MANUFACTURING, AND CONTROL (CMC) REVIEWERS OF HUMAN SOMATIC CELL THERAPY INVESTIGATIONAL NEW DRUG APPLICATIONS (INDS*)* 20-21 (April 2008), *available at* http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Xenotransplantation/ucm092705.pdf [hereinafter *SCT Guidance*].

[30] *See*, *e.g.*, Marcia Barinaga, *Fetal Neuron Grafts Pave the Way for Stem Cell Therapies*, 287 SCIENCE 1421 (2000); BIOLOGICAL RESPONSE MODIFIERS ADVISORY COMMITTEE, BRMAC MEETING # 27: HUMAN STEM CELLS AS CELLULAR REPLACEMENT THERAPIES FOR NEUROLOGICAL DISORDERS, at 1 (Draft 2000).

[31] *See, e.g.*, *SCT Guidance*, *supra* note 29, at 1, 13-18; *Guidance for Industry: Gene Therapy Clinical Trial--Observing Participants for Delayed Adverse Events*, F.D.A., (Recommendations Nov. 2006) http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/CellularandGeneTherapy/ucm072957.htm. FDA action is particularly evident in the case on somatic cell therapy for cardiac diseases, and this therapy would include stem

In sum, though every stem cell product does not fit nicely into a single FDA product classification, we are able to narrow the classification to the most likely candidates: biological products and combination products. This narrowing of the possibilities means that the most relevant product liability precedents will come from cases involving biologics and combination products, and to a lesser degree from drug and device cases. Even so, because stem cell products do not fit perfectly into the FDA classes that seem the most plausible, one should take care not to give any particular precedent too much weight.

III. EXISTING PRODUCT LIABILITY RULES AND STEM CELL PRODUCTS

From the above classifications, I move to the law of tort. Here, the central issues are two-fold: how current law deals with harm caused by medical products (and, by implication, how it would presumably deal with stem cell products) and how the law should deal with harm caused by stem cell products. Fault liability leaves the loss where it lies unless the victim can show that the manufacturer was negligent. Strict liability places the loss on the product's maker, provided that the victim can show that the defective product caused the harm. Distributionally, fault liability transfers wealth from victims to product makers, and strict liability does just the opposite. From the standpoint of the efficient allocation of resources,[32] it makes sense to place the loss on the party in the best position to reduce the harm from defective products. This party is often termed the "cheapest cost avoider." Unfortunately, it is often difficult to tell which party is the cheapest cost avoider, and it is debatable whether allocative efficiency should trump undesirable distributional consequences.

To grapple with these issues, I sketch the basic product liability rules for drugs, medical devices, and biologic-device combination products. I then compare stem cell products to partly analogous products (gene therapies, blood products, and vaccines) and distill the likely implications of existing law for harm caused by stem cell products. Later, in Part V, I discuss legal policy and what the law on liability for defective stem cell products should be.

A. Basic Product Liability Rules for Drugs and Medical Devices

The basic rules for drugs and medical devices build on the general framework for product liability. The framework finds lucid expression in the

cells. *See* Draft Guidance for Industry: Somatic Cell Therapy for Cardiac Disease, 70 Fed. Reg. 14,992, 14,992 (Apr. 2, 2009).

[32] For the moment I put to one side difficulties with specifying and applying a concept of efficiency. *See infra* Part IV.

Restatement (Third) of Torts: Products Liability, published by American Law Institute in 1998. Commercial sellers and distributors are liable for harm caused by products that are defective in manufacture or design, or come without adequate instructions or warnings.[33] Potential liability exists both at the time of sale and for post-sale failure to warn or recall a defective product.[34] To recover damages, a plaintiff must establish a causal connection between the defect and the harm, and the defendant can set up some affirmative defenses.[35] Furthermore, though liability exists without regard to fault in the case of manufacturing defects, the situation is different in the case of design defects and defects in instructions and warnings.[36] The *Restatement* view is only that strict liability *may* apply if there are design defects or defects in instruction or warning.[37] For practical purposes, the *Restatement* is a regime of qualified strict liability.

Chapter 1, Section 6 of the *Restatement* distills the principal lines of product liability for "drugs" and "medical devices":

> § 6(a): A manufacturer of a prescription drug or medical device who sells or otherwise distributes a defective drug or medical device is subject to liability for harm to persons caused by the defect. . . .
>
> § 6(b): A prescription drug or medical device is defective if at the time or sale or other distribution the drug or medical device:
>
> (1) contains a manufacturing defect . . . ; or
>
> (2) is not reasonably safe due to defective design . . . ; or
>
> (3) is not reasonably safe due to inadequate instructions or warnings . . .
>
> § 6(c): A prescription drug or medical device is not reasonably safe due to defective design if the foreseeable risks of harm posed by the drug or medical device are sufficiently great in relation to its foreseeable therapeutic benefits that reasonable health-care providers . . . would not

[33] *See* R3D PRODUCTS LIABILITY, *supra* note 3, §§ 1, 2.

[34] *See id.* §§ 10, 11.

[35] *See id.* §§ 15, 17, 18. Section 18 also discusses what defendants cannot claim.

[36] *See id.* §§ 1 cmt. a, 2 cmt. a, 2 cmt. n, 2 reporters' note, cmt. a.

[37] *See id.*

> prescribe the drug or medical device for any class of patients.
>
> § 6(d): A prescription drug or medical device is not reasonably safe . . . if reasonable instructions or warnings regarding foreseeable risks of harm are not provided to:
>
> (1) prescribing and other health-care providers who are in a position to reduce the risks of harm in accordance with the instructions or warnings, or
>
> (2) the patient, when the manufacturer knows or has reason to know that health-care providers will not be in a position to reduce the risks of harm in accordance with the instructions or warnings.[38]

Sections 6(a) and 6(b) give basic rules. Section 6(c) is an exception to the traditional rule that drug and device manufacturers are liable only for defects or selling products without adequate warnings or instructions. The § 6(c) exception is the "unavoidably unsafe" rule. A drug or device is considered to be defective only if it does not provide benefit to *any* class of patients. This exception is sometimes the premise of an entire product liability case against the manufacturer. Section 6(d)(1) is the "learned intermediary" rule. Physicians, for example, count as learned intermediaries. In cases brought against drug or device manufacturers based on "failure to warn" claims, this rule is often a basis for determining whether the manufacturer has met its obligation and is given summary judgment or a directed verdict. However, § 6(d)(2) creates an exception to the learned intermediary rule. It requires a direct warning to the patient where the circumstances described are present.[39]

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[38] R3D PRODUCTS LIABILITY, *supra* note 3, §§ 1, 2.

[39] *Id*. Section 6 nowhere defines "medical device." The closest it comes is in the last sentence of § 6(a): "A prescription drug or medical device is one that may be legally sold or otherwise distributed only pursuant to a health-care provider's prescription." *Id*. (suggesting, oddly, that an over-the-counter device, such as an ear syringe or a blood-glucose monitor, might not qualify as a "medical device"). Later, § 19 states that "human blood and human tissue, even when provided commercially, are not subject to the rules of this Restatement," and a comment indicates that this provision stems from the widespread adoption of blood shield laws (see text in III.B.3 *infra* for description of blood shield laws). *Id*. § 19 cmt. c. Given that some stem cells products like hematopoietic stem cells might well count as blood products, and almost surely would count as tissue, the Restatement rules might not apply. *See infra* text accompanying notes 58-63. To avoid some problems of interpretation, it would be sensible for courts to understand "medical device" according to the definition in the FFDCA. 21 U.S.C. § 321(h) (2006). Other problems of interpretation

Numerous statutes now modify the product liability rules applicable to drugs and medical devices. There are also statutes that affect the rules applicable to biologics and combination products. I will come to some of these statutes shortly. For the moment, note that federal law preempts state tort law regarding product liability in the case of devices and some vaccines.[40] In most ways preemption is quite sensible, for it provides everyone with a uniform nationwide set of rules. One problem with federal preemption is that manufacturers can focus their lobbying efforts on Congress to the exclusion of state legislatures or state court judges, who might have more sensible positions.

B. Applying Existing Product Liability Law to Stem Cell Products

The beginning of wisdom, though not its end, is to compare plausible stem cell products to existing product liability categories. Most stem cell products are likely to be combination products, which consist of a biologic and a device in which the biologic dominates. So, I take my cue from product liability rules and cases that involve biologics primarily and consider only secondarily combination products that contain a device. Along the way I pick up statutes that modify standard rules of product liability law. I treat these matters under four headings: biologic-device combination products, gene therapies, blood products, and vaccines. I then distill the likely overall result for stem cell products under existing law.

1. Biologic-Device Combination Products

The ideal legal examples are biologic-device combination products in which only the biologic component is defective and causes harm. Failure of the device component is shielded from strict liability by federal preemption of any state law to the contrary.[41] A good illustration of a stem cell biologic-device

will remain, for example, whether stem cell combination products that contain a device and a biologic derived from human blood or tissue count as a "medical device" under the Restatement.

[40] Medical Device Amendments Act of 1976, Pub. L. No. 94-295, § 2, 90 Stat. 539 (1976) (codified at 21 U.S.C. § 360k (2006)). No state may establish a requirement for the safety or efficacy of a medical device that "is different from, or in addition to, any requirement applicable under [the FFDCA] to the device." 21 U.S.C. § 360k(a)(1) (2006). Common-law causes of action for strict liability impose "requirements" under sec. 360k and are therefore preempted by federal requirements for approval of a medical device. Medtronic, Inc. v. Lohr, 518 U.S. 470, 512 (1996) (O'Connor, J., concurring); Riegel v. Medtronic, Inc., 552 U.S. 312, 323-24 (2008).

[41] 21 U.S.C. § 360k (2006).

combination product is the CellBeads®-Biopolymer made by CellMed AG, a fully owned subsidiary of Biocompatibles International plc. As of December 2008, twenty stroke patients were being treated in a Phase I/II trial in Germany.[42] The biologic component consists of human adult mesenchymal stem cells from a healthy donor.[43] The device component consists of a mesh and alginate beads that encapsulate the stem cells.[44] Scientists genetically engineer the cells so that they synthesize a protein that has anti-apoptotic effects (i.e. guards against cell death), and they deliver the cells directly and continuously to the injury site for fourteen days.[45] The beads protect the stem cells from the recipient's immune system.[46] The mesh retrieves the beads after the treatment period.[47]

2. Gene Therapies

Gene therapy, the placing of a functioning gene into a patient's somatic cells, does not usually employ a delivery device. Its purposes are to give cells a new function and to rectify an in-born genetic error. To get the gene inside the cell that lacks a needed gene or has a defective gene, scientists generally use a viral vector, such as an adenovirus or a retrovirus.[48] Viral vectors usually cannot be sterilized or characterized to the same extent as a typical drug.[49] Gene therapy sometimes works, but on occasion the viral vectors prove toxic and cause harm or even death. The most notable calamity was the death of Jesse Gelsinger in 1999 as a direct result of gene therapy gone wrong.[50] Although the case settled for an undisclosed sum, the settlement amount is estimated to have been about $10 million.[51] There is some progress in using

[42] *First-Ever Treatment of Stroke Patient with Stem Cell Therapy Product*, ASCR NETWORK (Dec. 2, 2008), http://www.ascrnetwork.com/ascr-laboratory-membership/321-first-ever-treatment-of-stroke-patient-with-stem-cell-therapy-product.html.

[43] *Id*.

[44] *Id*.

[45] *Id*.

[46] *Id*.

[47] *Id*.

[48] *See, e.g.*, Gene Therapy Net, *Retroviral Vectors* http://www.genetherapynet.com/viral-vectors/retroviruses.html (last visited Nov. 23, 2011).

[49] *See, e.g.*, Laura K. Aguilar & Estuardo Aguilar-Cordova, *Evolution of a Gene Therapy Clinical Trial: From Bench to Bedside and Back*, 65 J. NEURO-ONCOLOGY 307 (2003).

[50] *See, e.g.*, Lynn Smith & Jacqueline Fowler Byers, *Gene Therapy in the Post-Gelsinger Era*, 4 HEALTHCARE L. ETHICS & REG. 104 (2002).

[51] Jim Smith, *Hospitals, Docs Settle with Feds in Gene-Therapy Death*, PHILA. DAILY

nonviral vectors in gene therapy but their ultimate success is far from assured.[52] On the whole, gene therapies, marked by early hype, have disappointed physicians and patients over the last two decades.

There are almost no reported legal cases and few legal articles on product liability for harm caused by gene therapy. One article reiterates the usual doctrine without targeting it perceptively to the special case of gene therapy.[53] Yet the article does make the useful point that federal preemption for medical devices does not apply to biologics such as gene therapies.[54] Judith A. Cregan offers a more probing analysis.[55] She does not attempt to claim that, because gene therapy is so wondrous, Congress should prohibit strict liability for harm it causes. Instead, she would limit strict liability to "manufacturing defects and failure to warn of known or reasonably knowable side effects."[56] She would, however, have Congress bar strict liability for design defects in human gene therapy. Her reasoning is that strict liability here would be "oppressive,"[57] but she does not explain why it would be so.

Although gene therapy is not fully parallel to stem cell products, Cregan is on to something that merits further exploration. Safety is uncertain in the case of gene therapy. It is especially uncertain in the case of stem cell products. Given this partial parallel, the fear of strict liability could frighten makers of stem cell products away from the market.

3. Blood Products

Some stem cell products are comparable to blood products. The term

NEWS, Feb. 10, 2005, at 24; Marie McCullough, *Lawyer Sees His Role as Warning to Clinical Researchers*, PHILA. INQUIRER, May 20, 2002, at D4. Additionally, the University of Pennsylvania and the Children's National Medical Center agreed to pay more than $1 million to the government to settle civil fraud accusations in connection with Gelsinger's death. *Settlement Is Reached in Fatal Experiment,* N.Y. TIMES, Feb. 10, 2005, *available at* http://query.nytimes.com/gst/fullpage.html?res=9F0DE2D6163AF933A25751C0A9639C8B63.

[52] *See, e.g.*, T. Niidome & L. Huang, *Gene Therapy Progress and Prospects: Nonviral Vectors*, 9 GENE THERAPY 1647 (2002).

[53] Wilson Huhn, *Three Legal Frameworks for Regulating Genetic Technology*, 19 J. CONTEMP. HEALTH L. & POL'Y 1, 10-11 (2002).

[54] *Id.*

[55] Judith A. Cregan, *Light, Fast, and Flexible: A New Approach to Regulation of Human Gene Therapy*, 32 MCGEORGE L. REV. 261, 275-77, 287 (2000).

[56] *Id.* at 287 (citing Brown v. Superior Court (Abbott Laboratories), 751 P.2d 470, 483 n.12 (Cal. 1988)).

[57] Cregan, *supra* note 55, at 287.

"blood products" includes whole blood, blood plasma, platelets, and factors of different sorts. As of January 2010, fifty states and the District of Columbia had a blood shield law that exempts hospitals, medical providers, blood banks, and other entities from strict liability when obtaining, preparing, injecting, transplanting, or otherwise using blood or components thereof.[58] In *Smith v. Cutter Biological, Inc.*,[59] a hemophiliac contracted HIV from injections of Factor VIII. Factor VIII is a protein that helps blood to coagulate.[60] The court determined that Factor VIII is a component prepared from blood and falls within the Hawaii Blood Shield Law.[61] As a result, there was no liability for those entities listed when a disease is transferred through blood unless the transfer occurred due to negligence.[62] Relatedly, the Connecticut Supreme Court held that the state's blood shield statute regards blood not as a commodity subject to sale but a *medical service*.[63] Patients injured from transfusions can bring claims based on negligence, but not strict liability.

For two reasons, statutes and cases pertaining to blood and blood products have only limited relevance to the appropriate legal treatment of stem cell products. First, the statutes and cases should cover, at most, only the functionally similar subset of stem cell products: hematopoietic stem cells—whether obtained from hESCs, bone marrow, or umbilical cord blood—and more committed cells and products derived from them. For instance, blood shield statutes could apply to hESC-derived hematopoietic stem cells just as they do to cord blood. Again, hESC-derived Factor VIII could be covered provided that the safety and effectiveness of Factor VIII so derived are confirmed. Hence the Hawaii statute as interpreted in *Cutter Biological*, or any equivalent statute, could govern these examples but not such possible stem cell products as hESC-derived cardiomyocytes, retinal cells, or neural progenitors that are not blood components.

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[58] Forty-nine states have had blood shield statutes. New Jersey and the District of Columbia achieve the same result by judicial decisions. *See* Jason L. Williams, Note, *Patient Safety or Profit: What Incentives Are Blood Shield Laws and FDA Regulations Creating for the Tissue Banking Industry?*, 2 IND. HEALTH L. REV. 295, 304 (2005). Williams states, incorrectly, that Vermont had no statute on this matter as of 2004. In fact, it has had one since 1990. VT. STAT. ANN. tit. 9A § 2-108 (1994).

[59] 823 P.2d 717 (Haw. 1991). *See also infra* note 197.

[60] *Id*. at 721-22.

[61] *Id*. at 722.

[62] *Id*. at 723.

[63] Zichichi v. Middlesex Mem'l. Hosp., 528 A.2d 805, 808 (Conn. 1987). *See also supra* note 39.

Second, it is premature to use the service-not-product maneuver to shield makers of most stem cell products from liability without fault. The safety and effectiveness of the whole blood supply in the United States are quite high. But the safety and effectiveness of most eventual stem cell products will remain unknown for many years. It is too early to give their manufacturers a shield against liability without fault until we have a better grasp of the disincentive effects of strict liability on manufacturers.

One can drive this second point home by elucidating the costs of the service-not-product move. For blood products, blood shield statutes make manufacturers and distributors liable only for negligence, and thus limit their liability more than typical federal and state product liability rules do. This limited liability reduces the insurance and legal costs for manufacturers and distributors. In turn, lower costs of production and distribution usually lead to a larger supply of blood products on the market and lower prices for them to patients. Consequently, some patients who would not have been able to afford blood products and related therapies under a product-liability system can afford them under a negligence system, and patients who would have been able to afford them under either system will pay less for them. However, both categories of patients will face higher safety risks unless manufacturers and distributors spend a socially efficient amount on safety measures under a negligence system.

These patients can hedge their increased safety risks if they have health insurance provided by their employers, the government, or private contracts with insurers. In the event that something goes wrong with a blood product in the absence of negligence, health insurance could cover the additional medical expenses. But patient deaths are irreversible. Even in cases where most harm can be undone, some patient morbidity would often result. Patients who are unable to hedge these higher safety risks will in effect have to bear these risks full on, which, of course, they would likely be willing to do in order to receive potential life-saving blood products. In effect, they are paying-with-risk. The broader point about higher safety risks and the narrower points about hedging these risks and paying-with-risk apply *mutatis mutandis* to stem cell products.

This familiar picture of blood products, though, becomes muddier in other respects once one looks at most anticipated stem cell products—that is, all stem cell products that are not blood products. The picture is muddier for various reasons. Only in time will we know which stem cell products will become available. If the law treats these products as products rather than services, the foregoing analysis will be largely inapplicable. And if health insurers regard some or all of these stem cell products as experimental, they might be unwilling to pay for them, which would preclude insured patients

from hedging their safety risks in the manner described earlier.

4. Vaccines

As the previous discussion of the FDA classification scheme brought out, some stem cell products share some characteristics with vaccines. Because vaccines involve the insertion of biological products into the human body, the risks associated with biologics that cannot be fully controlled can be similar for both vaccines and some stem cell products. A common profile for vaccines, however, is great effectiveness in preventing the targeted disease in vaccinated individuals, modest likelihood of minor side effects (for example, low-grade fever, rash or soreness at the injection site), and rare major or catastrophic side effects.

Still, there are four salient dissimilarities between vaccines and stem cell products. First, vaccines are likely to be more vulnerable to product liability suits than are stem cell products. Vaccines are generally given to healthy individuals, whereas sick persons would be candidates for stem cell products. Injured persons are more likely to attribute the cause of injury to a vaccine if they are otherwise healthy and less likely to attribute the cause to a stem cell product if they are already sick. Second, there is no known common risk profile for stem cell products. Because of the wide range of uses for these products, there might not ultimately be a *common* profile. In contrast, the risk profile of most vaccines is usually known. Third, and somewhat related to the above dissimilarities, stem cell side effects could also occur long after the stem cell products were used. Unlike for vaccines, a long delay in the injury would complicate proving causation. Fourth, vaccines and stem cell products differ from the perspectives of public goods and externalities. Vaccines are preventive measures often administered at a relatively young age, and vaccines usually have positive externalities (such as decreases in health-care costs and in the transmission and severity of disease) and, if vaccination is extremely widespread, occasionally the general benefit of eliminating a particular disease, such as smallpox, altogether.[64] Stem cell products are likely to be used to treat existing diseases or conditions and to have fewer and smaller positive externalities.[65]

(a) The Common Law Model. This model applies the principles of Chapter 1, Section 6 of the *Restatement* to vaccines. Especially important principles

[64] Bryan L. Boulier et al., *Vaccination Externalities*, 7 B.E. J. ECON. ANALYSIS & POLICY 1, 1 (2007).

[65] These products could have some positive externalities, such as eliminating or at least reducing the costs of chronic diseases and thereby decreasing health-care costs.

here are the intersection of the duty to warn with the "learned intermediary" rule and the "unavoidably unsafe" rule.[66] We can see their application in the following cases.

In *Campagna v. American Cyanamid Company*, an infant of five months received an oral polio vaccination.[67] Not long afterward, he was hospitalized because of a high fever and an inability to move his left leg.[68] The diagnosis was "poliomyelitis, meningoencephalitis, and left leg paralysis."[69] The patient, his mother, and his guardian sued the manufacturer on the ground that the vaccine was defective because it did not meet federal standards.[70] The plaintiffs alleged that the defendant did not adequately warn them about the dangers of a non-compliant vaccination.[71] They also alleged that the defendant released vaccines that did not comply with these standards.[72] Although the defendant had received summary judgment in the lower court, the appellate court held that there was evidence that some shipments of the vaccine failed to comply with federal standards.[73] Because of this evidence, there could be a "failure to warn" claim because the package insert from the oral polio vaccine asserted that the vaccine was in accordance with FDA regulations.[74] But the infant's physician, a learned intermediary who was unaware of the possible non-conformity of the vaccine, would have had no basis for declining to use it.[75]

There is a lesson in *Campagna* for some stem cell products. Most shipments of the oral polio vaccine were in compliance. But some were not due to higher virulence in animal testing; that was why the failure to warn claim could be brought to trial. The complexity of the vaccination system—including having to test virulence on animals to ensure that the levels are adequate — was required because of the unpredictability of these biological

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[66] *See* R3D PRODUCT LIABILITY, *supra* note 3, §§ 6(b)(3), 6(d)(1), and 6(c), respectively. *See also* Edmund W. Kitch, *Vaccines and Product Liability: A Case of Contagious Litigation,* REGULATION, May/June 1985, at 11.

[67] 767 A.2d 996 (N.J. Super. App. Div. 2001).

[68] *Id.* at 997.

[69] *Id.*

[70] *Id.*

[71] *Id.*

[72] *Id.*

[73] *Id.* at 998.

[74] *Id.* at 1005-07.

[75] *Id.* at 998. The appellate court held only that American Cyanamid was not entitled to summary judgment. It remanded the factually disputed issues for further proceedings.

products. Stem cell products may have similar difficulties because the purity of the stem cells and their ability to develop into the desired differentiated cells are critical to whether they are successful or create a risk to the human body. Owing to these similarities, vaccination litigation is a possible model for some stem cell products.

In *Toner v. Lederle Laboratories*,[76] a three-month old boy received a vaccine known as Tri-Immunol to immunize against diphtheria, pertussis, and tetanus. Afterwards he developed transverse myelitis, which caused permanent paralysis from the waist down.[77] The interesting legal issue is the application of the "unavoidably unsafe" rule to this product. The court said that with new or experimental drugs, there is lack of time and opportunity to gain enough medical experience to ensure safety.[78] Risks created in the process of trying to make products safer may be justifiable in the case of a dreadful disease with no alternatives yet available.[79] *Toner* stands for the proposition that if there is not yet a safer alternative available at the time of distribution, then the comparison must be between the risks of the vaccine and the risks of the disease it is designed to prevent. The court held that strict liability should not be imposed on the manufacturer, but that negligence claims should be allowed to compare the risks and determine whether safer alternatives were feasible at that time.[80]

If the proposition for which *Toner* stands were extended to stem cell products, the court's interpretation of the "unavoidably unsafe" doctrine could provide some shelter to the makers of these products. In essence, they would have a shield against strict liability so long as risks of the stem cell products are not graver than the risks of the disease or condition to be treated. If the disease were Alzheimer's, Parkinson's, diabetes, or severe cardiomyopathy, the shield would be quite strong.

Even so, for several reasons the legal situation is not likely to wholly satisfy makers of stem cell products. To begin, it does not protect them against liability for negligence. Next, there is no assurance that courts will extend the *Toner* principle from vaccines to stem cell products, or that state or federal legislatures will refrain from interfering with the extension. Furthermore, there is the great dissimilarity pointed to earlier. Vaccines generally, and diphtheria-pertussis-tetanus vaccines in particular, protect most of those vaccinated quite successfully with an extremely low rate of severe side effects. We know little

[76] 732 P.2d 297 (Idaho 1987).

[77] *Id*. at 299.

[78] *Id*. at 304-05.

[79] *Id*. at 306.

[80] *Id*.

about the safety and effectiveness of stem cell products except for those derived from hematopoietic stem cells.

(b) The National Vaccine Injury Compensation Program Model. This program, created in the mid-1980s and known as the VICP, is a no-fault alternative to the product liability tort approach.[81] It applies to a broad range of vaccines given to children.[82] To obtain compensation, a child's representative must establish one of the following: the child had a listed injury, the vaccine made an existing condition much worse, or the vaccine caused the condition or an unlisted injury.[83] The child's petition goes to the Secretary of Health and Human Services and then to a special master of a federal court.[84] Only if the child's representative rejects the court's decision may he or she sue the maker of the vaccine in federal or state court.[85]

The VICP is neither entirely successful for children's vaccines nor ready for prime time for stem cell products. As Lars Noah points out, the VICP has not solved all problems of vaccine supply.[86] One reason may be that its preemption of state law is incomplete.[87] As to constructing a VICP-like program for stem cell products, any such proposal is premature. The specter of product liability prompts makers of these products to be careful, and no one yet knows whether stem cell products will be sufficiently safe and effective to merit the special favor of a no-fault regime.

C. Conclusion on Product Liability under Existing Law

At this time, the principles enunciated in Chapter 1, Section 6 of the *Restatement* will, with minor adjustments, probably govern product liability for

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[81] *See* National Childhood Vaccine Injury Act, Title III of Pub. L. No. 99-660, 100 Stat. 3755 (1986) (effective Oct. 1, 1988), *codified at* 42 U.S.C. § 300aa (2006).

[82] Specifically, the VICP covers all those vaccines that the Centers for Disease Control and Prevention recommend for children. The current list is available at http://www.hrsa.gov/vaccinecompensation/vaccinetable.html (last visited December 2, 2011). It includes vaccines against trivalent influenza, measles, mumps, rubella, polio, tetanus, pertussis, hepatitis A and B, and varicella among others.

[83] 42 U.S.C. § 300aa-11(c)(1) (2006).

[84] 42 U.S.C. § 300aa-11(a)(1) (2006).

[85] James M. Wood et al., *Product Liability Protection for Stem Cell Research and Therapies—A Proposal,* 18 Health L. 1, 8-9 (2005).

[86] Lars Noah, *Triage in the Nation's Medicine Cabinet: The Puzzling Scarcity of Vaccines and Other Drugs*, 54 S.C. L. REV. 741, 761 (2002).

[87] *See* Wood et al., *supra* note 85, at 1, 9.

stem cell products.[88] The basic scheme, then, would be qualified strict liability for stem cell products that are defective in design or manufacture or have inadequate instructions or warnings.[89] The "unavoidably unsafe" rule and the "learned intermediary" rule would give some relief to manufacturers that make their products as safe as possible.[90] Because almost all stem cell products will be biologics or biologic components of combination products, the stringent approval standards for biologics, and especially cellular biologics, should apply.

Although the *Medical Device Amendments Act* gives substantial shelter to class III medical devices, such as cardiac devices and neurostimulation systems,[91] this shelter is unlikely to extend to the stem cell biologic component of a combination product. Furthermore, a salient dissimilarity between vaccines and stem cell products subverts the transfer of either of the models—the common law or the no-fault VICP—for vaccines to stem cell products. The dissimilarity is that vaccines have a track record of great effectiveness, modest probability of minor side effects, and rare catastrophic side effects, whereas we have little information on the safety and effectiveness of stem cell products, for very few stem cell products are on the market. For similar reasons, these products will probably not have the muscular protection against strict liability accorded to whole blood and assorted blood products, save perhaps for hematopoietic stem cell transfusions.

IV. ECONOMIC CONSIDERATIONS FOR A STEM CELL LIABILITY REGIME

A liability regime for stem cell products should take into account the ways in which economic incentives will affect the manufacture, sale, and use of stem cell products. Thus, in this part, I aim to provide a feasible economic framework to situate stem cell liability rules. In the first section, I deploy a standard neoclassical economic analysis of liability for stem cell products. In

[88] R3D PRODUCTS LIABILITY, *supra* note 3, §§ 1-8.

[89] *See id.* §§ 6(a)-(b).

[90] *See id.* §§ 6(c)-(d)(1).

[91] No state may establish a requirement for the safety or efficacy of a medical device that differs from or adds to the requirements of the FFDCA. 21 U.S.C. § 360k(a) (2006). Courts have applied this provision to preempt a state law requirement that conflicts with a federal requirement related to medical devices. *See, e.g.*, Riegel v. Medtronic, Inc., 552 U.S. 312, 323-24 (2008) (tort claims against the manufacturer of a cardiac balloon catheter preempted by federal statute); McMullen v. Medtronic, Inc., 421 F.3d 482, 484, 490 (7th Cir. 2005) (tort claims against the manufacturer of an implanted electronic tremor control system preempted by federal statute).

the second section, I supplement and alter that analysis. My reasons for doing so rest on problems involving rationality, inadequate information, behavioral economics, game theory, and the foundations of economics. These problems stalk neoclassical economics at its core.

A. Neoclassical Economics

1. A Neoclassical Approach Stated

An older classical economic analysis, associated especially with the early work of Frank H. Knight,[92] distinguished between risk and uncertainty. Knight understood *risk* as a measurable quantity and *uncertainty* as an unmeasurable quantity.[93] He was well aware that in standard English, "risk" has to do with unfavorable or undesirable contingencies, and he believed, incorrectly in my opinion, that "uncertainty" has to do only with favorable or desirable contingencies.[94] But Knight was not a guardian of English usage or a proto-ordinary-language philosopher, and it was the distinction between measurable and unmeasurable quantities pertaining to the occurrence of future events that fired his imagination regarding the analysis of profit. Risk, he thought, was a matter of statistical probabilities or, in some instances, was knowable *a priori*.[95] Uncertainty, he believed, was stochastic, and could be no more than a matter of estimation.[96] Most economists today would recognize Knight's distinction as involving, not a difference in kind, but a difference in degree, and the ensuing discussion follows the contemporary economic understanding.[97]

Mark A. Geistfeld gives a useful neoclassical model of risk pertaining to product liability,[98] which I adapt to stem cell products. Consider, for instance, the use of hESC-derived insulin-producing cells to treat Type 1 diabetes.[99]

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[92] FRANK H. KNIGHT, RISK, UNCERTAINTY, AND PROFIT (1921).

[93] *Id*. at 19-20, 233.

[94] *Id*. at 233.

[95] *Id*.

[96] *See id*. at 197-263 (elaborating on the distinction between risk and uncertainty).

[97] *Cf*. JACK HIRSHLEIFER & JOHN G. RILEY, THE ANALYTICS OF UNCERTAINTY AND INFORMATION 9-10 (1992) (maintaining that Knight's distinction is "sterile" and that probability is "simply degree of belief" (emphasis omitted)).

[98] Mark A. Geistfeld, *Product Liability*, *in* TORT LAW AND ECONOMICS 287, 287-340 (Michael Faure ed., 2009). Geistfeld introduces some non-neoclassical elements into his account, which for the moment I ignore.

[99] *See supra* text accompanying note 10.

The "full price" of these insulin-producing cells is a function of the amount invested in safety and effectiveness.[100] To simplify matters, attend now only to safety. An "optimum level of safety" is an equilibrium point in a competitive market in which consumers are rational and have perfect information, and there are no transaction costs. Here, according to Geistfeld,[101] the full price **P** of these cells is the sum of the purchase price *p,* the investment by the producer—in this case, ViaCyte[102]—in safety *s,* and the expected accident cost *r(s)L*. The expected accident cost is the mathematical product of the injury cost *L* (say, the cost of a diabetic coma) and the probability (risk) that the stem cell product will cause this injury at this level of investment in safety *r(s)* (risk as a function of safety):

$$\mathbf{P} = p + s + r(s)L$$

Given that rational consumers will choose a stem cell product on the basis of **P** rather than *p*, and given a perfectly competitive market with perfect information, it does not matter whether the seller or the consumer bears the loss of injury. In either case, the seller will provide the optimal amount of safety *s** as defined by:

$$1 = -r'(s^*)L$$

Thus, "the seller invests in safety until the last dollar spent reduces expected injury costs by one dollar."[103]

Anyone who subscribes to Geistfeld's unaltered neoclassical model would find the particular liability regime of the *Restatement (Third) of Torts: Products Liability* beside the point. It would not matter who bore the risk of injury. Neither would it matter whether strict liability or negligence governed. Whether under strict liability or negligence, in the absence of transaction costs, the liability rule would not affect the amount invested in safety. Further, the unavoidably unsafe rule and the learned intermediary rule would be otiose. Both would be unnecessary exceptions to strict liability in a model where consumers would have perfect information of all risks. Consumers would know the risk a particular product posed to them in light of their own unique health profile. In such a perfectly competitive market with rational and

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[100] *Cf*. Geistfeld, *supra* note 98, at 289 (defining true cost in terms of safety only). Later on the same page, Geistfeld seems to interpret *s* as "the amount of safety and warranty coverage." It would appear that this coverage involves a warranty of safety only, not a combined warranty of safety and effectiveness. For a brief discussion of product warranties, insurance costs, and warranty liability, see *id*. at 295-98.

[101] *Id*. at 289.

[102] *See Clinical Application*, *supra* note 10.

[103] Geistfeld, *supra* note 98, at 290.

informed consumers, an unqualified regime of strict liability would suffice.

2. Shortcomings of a Neoclassical Approach

Rarely, however, are markets perfectly competitive. Sellers and consumers of stem cell products, such as hESC-derived insulin-producing cells, almost never have perfect information. Their rationality is frequently suspect, and indeed what one means by "rationality" is open to doubt. Thus investments by manufacturers, such as ViaCyte, in safety can be, and almost always are, suboptimal. Suboptimality occurs for many reasons. The true cost of injury *I* often differs from the monetary injury cost *L* plugged into the formulas above.[104] There is no competitive market—only a regulated market, if you will—for stem cell products, because the FDA is responsible for "assuring the safety, efficacy, and security" of drugs, devices, biologics, and combination products.[105] Competition among the manufacturers of stem cell products is inhibited and suffers from limited entry, because FDA trials and studies demand enormous investment from manufacturers.[106] Temporary patent monopolies and captive consumers[107] further limit competition. If a market is not perfectly competitive, then manufacturers may well be able to sell stem cell

[104] It is difficult to measure monetary compensation for physical injuries, loss of life, and loss of consortium. *See, e.g.*, David J. Mark, Comment, *Liability for Failure of Birth Control Methods*, 76 COLUM. L. REV. 1187, 1201 (1976) (explaining some of the difficulties in measuring monetary compensation). Assigning a monetary value to pain and suffering is likewise difficult. *See, e.g.*, Mark A. Geistfeld, *Placing a Price on Pain and Suffering: A Method for Helping Juries Determine Tort Damages for Nonmonetary Injuries*, 83 CAL. L. REV. 773, 803-05 (1995) (articulating a way to reduce this difficulty).

[105] *What We Do*, FDA (Nov. 18, 2010), http://www.fda.gov/aboutfda/whatwedo/default.htm. The FDA-regulated market in the United States does not include price controls. *See* Mary K. Olson, *Pharmaceutical Regulation, in* 3 THE NEW PALGRAVE DICTIONARY OF ECONOMICS AND THE LAW 40, 41(Peter Newman ed., 1998) (contrasting the United States in this respect with some European countries).

[106] Pre-approval testing is limited; manufacturers abandon many products for financial reasons. The average pre-approval cost to bring a new drug to market in 2003 was an estimated $802 million. Joseph A. DiMasi et al., *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 151 (2003).

[107] The demand for life-saving products is likely to be relatively inelastic. *See, e.g.*, Awad Mataria et al., *Demand Assessment and Price-Elasticity Estimation of Quality-Improved Primary Care in Palestine: A Contribution from Contingent Valuation Method*, 16 HEALTH ECON. 1051 (2007) (explaining the reasons for demand inelasticity).

products even to perfectly informed consumers at supracompetitive prices.[108]

In the event that both perfect competition and perfect information are lacking, and certainly if transaction costs exceed zero, then which liability rule the legal system uses for stem cell products—say, hESC-derived insulin-producing cells—makes a difference. If the system imposes strict liability for defective insulin-producing cells, plaintiffs still have to prove that a defect existed in order to recover.[109] They also need to rebut any defenses set up by manufacturers or other defendants that invoke the unavoidably unsafe rule or the learned intermediary rule.[110] If the legal system uses a negligence rule, plaintiffs have to establish or rebut all of the foregoing and prove that the manufacturers and other defendants were negligent.

The inclusion of transaction costs, as the middle third of Coase's famous article on social cost does, indicates that a socially efficient result will occur only if the legal system directs the judge to apply precisely the right liability rule.[111] That rule might not be either strict liability or negligence liability but some highly qualified intermediate rule. If the legal system does not pick exactly the right liability rule, then either the transaction costs will exceed the increase in value from rearranging the legal outcome, which means that the transaction will not be entered into, or the transaction costs will not exceed that value, which means that the transaction will be entered into but social resources will be consumed in carrying out the transaction.[112] This high-wire act threatens to create "too much uncertainty about the legal position itself,"[113] which increases inefficiency.[114]

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[108] Geistfeld, *supra* note 98, at 290. For estimates of the cost of drugs, which may give some insight into the potential cost of stem cell products, see Christopher P. Adams & Van V. Brantner, *Estimating The Cost Of New Drug Development: Is It Really $802 Million?*, 25 HEALTH AFF. 420 (2006); Dimasi et al., *supra* note 106.

[109] R3D PRODUCTS LIABILITY, *supra* note 3, § 6.

[110] *Id*. §§ 6(c), 6(d)(1). *See supra* text accompanying notes 38-39.

[111] R.H. Coase, *The Problem of Social Cost,* 3 J.L. & ECON. 1, 15-28 (1960).

[112] *Id*.

[113] *Id*. at 19.

[114] I leave aside, as not directly in point, Austrian-school criticisms of efficiency understood as Kaldor-Hicks potential compensation with regard to individual preference-satisfaction. *See, e.g.,* FRIEDRICH A. VON HAYEK, THE COUNTER-REVOLUTION OF SCIENCE 29-30 (1952) (contending that the social scientist has little access to the data behind human actions because this data lies "in many individual minds"); Mario J. Rizzo, *The Mirage of Efficiency*, 8 HOFSTRA L. REV. 641, 642 (1979-1980) (maintaining that "tremendous information requirements . . . make pursuit of the efficiency norm impractical").

Nor do I rehearse the standard difficulties with revealed preference theory. S*ee*, *e.g.*,

Moreover, even if one assumes perfect competition, perfect information, rationality and zero transaction costs, there are well-known difficulties with Coase's position.[115] It is not the case that the *same* efficient allocation of resources will always be achieved, whatever the legal rule. Different efficiency equilibria often correspond to different wealth distributions, and almost surely changes in the legal rule will over time redistribute wealth.[116] Nor is it evident that *an* efficient allocation of resources will result under the foregoing assumptions, whatever the legal rule. The usual meanings of individual "rationality"—such as maximizing utility, maximizing expected utility, adopting a maximin strategy—do not make this weaker claim true except in simple situations, for example, a two-person constant-sum game. In n-person variable-sum games, especially where n is very large, some contend that no agreed-upon understanding of rationality exists, and that it is no longer possible to work with standard assumptions of welfare economics.[117] Even if

STEPHEN R. MUNZER, A THEORY OF PROPERTY 196 (1990) (reviewing the basic difficulty); AMARTYA SEN, CHOICE, WELFARE AND MEASUREMENT 41-106 (1982) (exploring determinants of choice other than preferences).

[115] Hoffman and Spitzer, in two articles, draw attention to other implicit conditions required for the "truth" of Coase's theorem. Elizabeth Hoffman & Matthew L. Spitzer, *Experimental Tests of the Coase Theorem with Large Bargaining Costs,* 15 J. LEGAL STUD. 149, 149 (1986) (including "two agents to each bargain," "convex" production and profit or utility functions, a "costless court system," and "no wealth effects"); Elizabeth Hoffman & Matthew L. Spitzer, *The Coase Theorem: Some Experimental Tests,* 25 J.L. & ECON. 73, 73 (1982) (giving a similar but not identical list). Hoffman and Spitzer mainly argue that in experiments Coase holds up pretty well with just two agents to each bargain but less well with three agents per bargain, and even less well with up to forty agents per bargain. Note that a proposition is not a "theorem" unless it is demonstrated to be true, and merely "holding up pretty well" is not a demonstration. Moreover, Hoffman and Spitzer pay inadequate attention to the contested nature of rationality in bargains among many persons (say, $n > 100$).

[116] *See* Donald H. Regan, *The Problem of Social Cost Revisited,* 15 J.L. & ECON. 427, 433 (1972) (calling this aspect of Coase's position the "invariance thesis" and contending that it does not hold save in the case of redistribution of rents).

[117] *See id*. at 431 (calling this aspect of Coase's position the "efficiency thesis" and claiming that it is not obviously true). *Cf*. K. Basu, *On the Non-Existence of a Rationality Definition for Extensive Games*, 19 INT'L J. GAME THEORY 33 (1990) (analyzing a problem with defining rationality for extensive games (roughly, a noncooperative game in which the players seek refinements of Nash equilibria) and arguing that the problem has no solution); Kaushik Basu, *The Traveler's Dilemma: Paradoxes of Rationality in Game Theory*, 84 AM. ECON. REV. 391, 392-95 (1994) (arguing that "backward induction" creates a paradox in single-shot as well as repeated games); Ken Binmore, *Modeling Rational Players: Part I*, 3

one could, rational behavior by each individual would not guarantee collective rationality and socially-optimal choices.[118]

One can add many more bells and whistles to a neoclassical account of liability for stem cell products, and Geistfeld and others add them.[119] None of them, or all of them together, entirely solve the difficulties mentioned. Neither do they solve the problem that, for purposes of efficiency, stem cell products involve effectiveness as well as safety. Almost never can one maximize both. Dual maximands are frogs at the bottom of the barrel of a neoclassical account of product liability for defective stem cell products.

Once one realizes the shortcomings of a neoclassical approach, the liability regime outlined in the *Restatement (Third) of Torts: Products Liability* is no longer superfluous. Of course, it does not follow that the *Restatement* articulates the best possible approach to product liability for defective stem cell products. That is a matter one will be able to judge only after the ensuing investigation.

B. Neoclassical Accounts Supplemented and Altered

Given the infirmities of neoclassical accounts, one must supplement and alter them at least in the ways indicated below. This supplemented and altered account remains economic in character. But it includes a good many qualifications about rationality, tries to grapple with the world as it is in making timely decisions, addresses problems with the "folk wisdom" that often

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ECON. & PHIL. 179 (1987) (discussing multiple concepts of equilibrium and rationality in game theory). For legal applications, see DOUGLAS G. BAIRD, ROBERT H. GERTNER & RANDAL C. PICKER, GAME THEORY AND THE LAW (1994) [hereinafter BAIRD ET AL.].

[118] Cost-benefit analysis ("CBA") is a near cousin of neoclassical economics. Richard Revesz and Michael Livermore correctly argue that CBA need not be tied to an anti-regulatory agenda and that CBA is hardly the sole useful means of policy analysis. RICHARD L. REVESZ & MICHAEL A. LIVERMORE, RETAKING RATIONALITY: HOW COST-BENEFIT ANALYSIS CAN BETTER PROTECT THE ENVIRONMENT AND OUR HEALTH (2008). Like Kysar and Farber, I believe that CBA is less useful than Revesz and Livermore suggest. DOUGLAS A. KYSAR, REGULATING FROM NOWHERE: ENVIRONMENTAL LAW AND THE SEARCH FOR OBJECTIVITY (2010); Daniel A. Farber, *Rethinking the Role of Cost-Benefit Analysis*, 76 U. CHI. L. REV. 1355 (2009) (book review).

[119] *See* Geistfeld, *supra* note 98, at 291-92, 295-98, 309-20 (discussing consumer information, product warranties, insurance costs, different sorts of defects, and other matters). *See generally* KENNETH J. ARROW, ESSAYS IN THE THEORY OF RISK BEARING (1971); STEVEN SHAVELL, ECONOMIC ANALYSIS OF ACCIDENT LAW (1987); DANIEL F. SPULBER, REGULATION AND MARKETS (1989); W. KIP VISCUSI, REFORMING PRODUCTS LIABILITY (1991).

includes persistent biases and misguided heuristics for making decisions, and recognizes underlying difficulties at the intersection of game theory and welfare economics. The net result is that any economic analysis, to be useful in thinking about product liability for defective stem cell products, such as insulin-producing cells derived from hESCs, must differ sharply from neoclassical accounts.

(a) The Nature of Rationality. To treat rationality as always maximizing efficiency, preference-satisfaction, or wealth is misguided. In some cases, the desirability or moral suitability of the asserted maximand is questionable. Perhaps individuals ought to have different preferences from the ones they currently possess.[120] In opposition to Richard Posner, Ronald Dworkin powerfully argues that wealth may not be a value in the way that Posner's views require.[121] Sometimes the rational person does not maximize but "satisfices"—that is, chooses any action that guarantees a satisfactory outcome.[122]

(b) Bounded Rationality and Later Developments. Simon's idea of satisficing leads to a broader point pertaining to what economists often call "bounded rationality." Roughly, the term applies to an approach to behavioral economics that takes into account a decision maker's informational and computational limits in the effort to make rational choices, although precisely what this term covers varies across different authors. Simon himself defined a "principle" of bounded rationality in these words:

The capacity of the human mind for formulating and solving complex problems is very small compared with the size of the problems whose solution is required for objectively rational behavior in the real world—or even for a reasonable approximation to such objective rationality.[123]

Neoclassical economics makes occasional concessions to the infirmities of human thinking and information, but is less rigorous in this respect than are theories of bounded rationality. As the field has developed in the wake of

[120] *See*, *e.g.*, David Dolinko, *The Perils of Welfare Economics*, 97 NW. U. L. REV. 351, 368-78 (2002) (book review) (giving telling examples of adaptive preferences and preferences whose satisfaction harms the person who has them).

[121] Ronald Dworkin, *Is Wealth a Value?*, 9 J. LEGAL STUD. 191 (1980).

[122] *See, e.g.*, Herbert A. Simon, *A Behavioral Model of Rational Choice*, 69 Q.J. ECON. 99 (1955). The continuing interest in this part of Simon's work is evident in the articles printed in SATISFICING AND MAXIMIZING: MORAL THEORISTS ON PRACTICAL REASON (Michael Byron ed., 2004).

[123] HERBERT A. SIMON, MODELS OF MAN 198 (1957) (emphasis omitted). Simon's career work in this area is collected in HERBERT A. SIMON, MODELS OF BOUNDED RATIONALITY (1982, 1997) (3 vols.).

Simon's pioneering work, it has come to include efforts to frame mathematical models of bounded rationality,[124] debates over the nature of rationality,[125] and studies of human behavior by psychologists and economists who perform experiments that test the conformity of behavior with neoclassical views of rationality.[126]

Later developments are both theoretical and empirical. Theoretical writers on risk and uncertainty now differentiate between risk aversion and uncertainty aversion. The latter concept, also called ambiguity aversion,[127] applies to certain preferences for known risks over unknown risks. Using this concept in experimental economics and decision theory led to the Ellsberg problem.[128] In one version of the problem, a decision maker faces two urns. The first contains 50 red balls and 50 yellow balls, and the decision maker knows the mix. The second urn contains 100 balls colored either red or yellow but the decision maker does not know what the mix is. He or she will receive $10 for each red ball but nothing for each yellow ball. Almost every participant in the experiment chose the first urn, with its known risky payoff, rather than the second, with its unknown "ambiguous" payoff. Further, when the same urns were displayed and the payoffs were reversed (i.e. $10 for each yellow ball and nothing for each red ball), almost all participants again chose the first urn over the second.[129]

The choices of almost all decision makers in this experiment are inconsistent with expected utility theory. Having a strict preference for the first urn both (i) when the red ball has a positive payoff and (ii) when the yellow ball has a positive payoff would require the following belief: that the ratio of red to

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[124] *E.g.*, ARIEL RUBINSTEIN, MODELING BOUNDED RATIONALITY (1998). *But see* PAUL ANAND, FOUNDATIONS OF RATIONAL CHOICE UNDER RISK (1993) (expressing skepticism of axiomatic and mathematical modeling of subjective expected utility).

[125] *E.g.*, THE OXFORD HANDBOOK OF RATIONALITY (Alfred R. Mele & Piers Rawling eds., 2004); ROBERT NOZICK, THE NATURE OF RATIONALITY (1993); Basu, *On the Non-Existence*, supra note 117; Basu, *The Traveler's Dilemma*, *supra* note 117; Binmore, supra note 117.

[126] *See*, *e.g.*, David M. Kreps, *Bounded Rationality*, *in* 1 THE NEW PALGRAVE DICTIONARY OF ECONOMICS AND THE LAW 168, 169-71 (Peter Newman ed., 1998) (surveying some work regarding bounded rationality).

[127] Larry G. Epstein, *A Definition of Uncertainty Aversion*, 66 REV. ECON. STUD. 579 (1999).

[128] Daniel R. Ellsberg, *Risk, Ambiguity, and the Savage Axioms*, 75 Q.J. ECON. 643 (1962).

[129] William S. Neilson, *A Simplifed Axiomatic Approach to Ambiguity Aversion*, 41 J. RISK & UNCERTAINTY 113 (2010).

yellow balls and the ratio of yellow to red balls in the first urn exceeds the corresponding ratios in the second urn. This complex belief cannot be true.[130] Although the Ellsberg problem is sometimes called a paradox, it is not really paradoxical. Rather, it shows that experimental results are sometimes inconsistent with expected utility theory. In another experiment, theories other than expected utility were examined.[131] They included maximin, maxmax, minimax regret, and the Hurwicz alpha-criterion.[132] No clear consistency across test subjects could be found as to which of these theories, if any, were used by the subjects.[133]

These theoretical results have implications concerning product liability for defective stem cell products. First, when people face uncertainty, they tend not to maximize expected utility beyond simple risk aversion. In the aggregate, this behavior is an unfortunate result. Second, the methods people use to make decisions under uncertainty are imperfectly understood and seem to be inconsistent across individuals. The lack of predictable irrationality suggests that the impact of any attempt to sway behavior under ambiguity is itself unpredictable. Third, the uncertain product liability regime currently in place for stem cell products could well lead to unpredictable jury awards, which might deter producers from entering the market. It might be possible to create a new liability regime that both producers and consumers would prefer to the current regime.

Empirically, there is specific evidence of the limits of neoclassical rationality in health care choices. Patient decisions and the degree to which patients act rationally are influenced by their affective states. In particular, patients in so-called "hot states" "tend to underappreciate the extent to which their preferences and behavioral inclinations are influenced by their affective state; they typically believe that they are behaving more dispassionately than they actually are."[134] Moreover, being in a "hot state" increases a patient's willingness to act on his or her own short-term preferences.[135] Research in this

[130] *Id.*

[131] John D. Hey, Gianna Lotito & Anna Moffioletti, *The Descriptive and Predictive Adequacy of Theories of Decision Making Under Uncertainty/Ambiguity*, 41 J. RISK & UNCERTAINTY 81 (2010).

[132] *Id.*

[133] For simplicity's sake I ignore various efforts, such as using Choquet expected utility or info-gap decision theory, to show that the Ellsberg problem is not a problem after all.

[134] George Loewenstein, *Hot-Cold Empathy Gaps and Medical Decision Making*, 24 HEALTH PSYCHOL. S49, S49 (2005).

[135] *Id.*

area of psychology is highly relevant to the clinical world because patients often make medical decisions when they have received adverse news, are in pain or discomfort, are fearful, or are under stress from having to choose between multiple unattractive and complicated alternatives.[136] It is therefore unsurprising that patients in such difficult circumstances and "hot" affective states tend to make long-term decisions on the basis of their current, and often transient, feelings. They are prone to overreact to risks that are new and unfamiliar and underreact to familiar risks.[137]

(c) Heuristics and Biases. Preeminent among general work on heuristics and biases that contaminate rational choices are the contributions of Daniel Kahneman and Amos Tversky.[138] To cope with the surfeit of information available and the complicated choices that need to be made in a limited time based on that information, individuals often develop "heuristics"—roughly, rules of thumb or mental shortcuts. Sometimes these heuristics work tolerably well but at other times they prove unhelpful or even counter-productive. Biases produce the same results.[139] In the case of stem cell products, one might find some patients biased in favor of them ("I want to treat my Type 1 diabetes with the most advanced medicine and technology available") while other patients are biased against them ("I'd rather treat my Type 1 diabetes with the best-supported techniques currently available than roll the dice with a newer, sexier stem-cell product").[140]

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[136] *Id*. at S52.

[137] *Id*. *Cf*. Brian J. Cohen, *Is Expected Utility Theory Normative for Medical Decision Making?*, 16 MED. DECISION MAKING 1 (1996) (arguing that expected utility theory does not track actual choices under risk).

[138] *See, e.g.*, JUDGMENT UNDER UNCERTAINTY: HEURISTICS AND BIASES (Daniel Kahneman, Paul Slovic & Amos Tversky eds., 1982) (collecting articles by the editors and other figures in this area of research).

[139] Jeffrey J. Rachlinksi, *Cognitive Errors, Individual Differences, and Paternalism*, 73 U. CHI. L. REV. 207, 207 (2006) (emphasis omitted). The author makes the useful point that, "in certain limited circumstances," the parameters of cognitive ability, experience and training, and demographic variables might pick out those individuals who are better than others in avoiding cognitive errors. *Id*. That the legal system will be able to identify these individuals when deciding whether to use stem cell products falls well outside the limited circumstances, especially experience, that he describes. *Id*.

[140] Even those biased in favor of the most cutting-edge treatments might find that a given non-stem cell product is superior to a given stem cell product. *See, e.g.*, Raymond D. Lund et al., *Cells Isolated from Umbilical Cord Tissue Rescue Photoreceptors and Visual Functions in a Rodent Model of Retinal Disease*, 25 STEM CELLS 602 (2007) (reporting that umbilical-derived cells yielded large areas of photoreceptor rescue whereas mesenchymal

Without doubt the use of some heuristics is ineluctable, and here it makes sense to use heuristics that are both robust and fitting. A "robust" heuristic enables a person to make good predictions about future events. A "fitting" heuristic enables a person to make his or her decisions comport with past events.[141] Unfortunately, robust and fitting heuristics are sometimes hard to identify and use in patients' deliberations under pressure. Research indicates that when patients have to make trade-offs involving conflict, they frequently use heuristics that undermine their own interests and lead to errors in decision making.[142] In particular, research indicates that when patients face competing objectives and complex information, they are prone to over-weight precise and concrete variables and to under-weight vague and less comprehensible factors.[143] This finding is highly pertinent to patients' decisions about stem cell products. For the risks associated with these products are neither well known nor well understood, which may lead patients to misassess the risks in making decisions about using these products.[144]

Against this backdrop, one strategy is to use a precautionary principle. One can formulate a principle of this sort in different ways. Here I explore the principle suggested for use in medical contexts by David B. Resnik: "One should take reasonable measures to prevent or mitigate threats that are plausible and serious."[145] Resnik intentionally says *reasonable* rather than *rational*. Under expected utility theory, there is only one rational choice unless at least two choices have the same expected utility, which is rarely the case. In contrast, there often is more than one reasonable response to a particular threat.

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stem cells rescued smaller areas of photoreceptors).

[141] Gerd Gigerenzer, *Fast and Frugal Heuristics: The Tools of Bounded Rationality*, *in* BLACKWELL HANDBOOK OF JUDGMENT AND DECISION MAKING 62, 78-79 (Derek J. Koehler & Nigel Harvey eds., 2004).

[142] Judith H. Hibbard, Paul Slovic & Jacquelyn J. Jewett, *Informing Consumer Decisions in Health Care: Implications from Decision-Making Research*, 75 MILBANK Q. 395, 399 (1997).

[143] *Id.*

[144] Jeffrey J. Rachlinski, *The Uncertain Psychological Case for Paternalism*, 97 NW. U. L. REV. 1165, 1168 (2003) (emphasis added). Rachlinski argues persuasively that many legal scholars "overappl[y]" the contemporary psychology of judgment and choice and that the psychological evidence does not "support abandoning individual judgment *in every instance* in which people rely on a misleading heuristic." *Id.* His argument has scant application at this time to patients' decisions about stem cell products because the risks are so poorly understood.

[145] David B. Resnik, *The Precautionary Principle and Medical Decision Making*, 29 J. MED. & PHIL. 281, 289-90 (2004).

Here a threat is plausible, as distinct from probable, if there is some evidence for the existence of the threat, but not enough evidence to assign an objective probability to the threat.[146] Whether a threat is serious depends on two factors: potential for harm and irreversibility.[147] For instance, a threat that has great potential for harm, and cannot be reversed if it materializes, counts as a serious threat. Under Resnick's account, one first assesses the plausibility of a threat, and then, if it is plausible, its seriousness, and finally, if it is serious, the reasonableness of possible responses to the threat.[148] A "reasonable" response, in his view, is one that "is proportional to degree of the threat, consistent with other decisions, carefully weighs benefits and harms, and takes a realistic attitude toward the threat and its prevention."[149]

This strategy exhibits commendable good sense, but it is rather complicated to count as a heuristic. Its complexity makes it difficult for patients with grave illnesses or conditions to use when considering stem cell products. For individuals in pain, beset by fear and worry and perhaps incapable of carrying out a complex process of assessment even in the best of times, a precautionary principle might not prove very useful.

And yet, this principle might be highly useful for the designers and manufacturers of stem cell products. The designers and manufacturers have a relative advantage over patients in determining the risks of a product, calculating the risks of taking or not taking precautions, and implementing reasonable precautions. If this part of my analysis is correct, then a regime of qualified strict liability is apt to be more efficient than either a regime of negligence or unqualified strict liability. The qualified regime would, moreover, act as a corrective when patients have incomplete information or misperceive or improperly assess risk.[150]

(d) Game Theory and the Foundations of Welfare Economics. Earlier I mentioned Donald Regan's view, expressed in his perceptive article on Coase,

[146] *Id*. at 287.

[147] *Id*. at 289.

[148] *Id*. at 293-94.

[149] *Id*. at 294.

[150] This argument employs qualified strict liability to spur designers and manufacturers to use a precautionary principle. It does not follow that the FDA or other regulators should use such a principle directly. *Cf*. Richard B. Stewart, *Environmental Regulatory Decision Making under Uncertainty*, *in* 20 AN INTRODUCTION TO THE LAW AND ECONOMICS OF ENVIRONMENTAL POLICY: ISSUES IN INSTITUTIONAL DESIGN 71, 71 (Timothy Swanson ed., 2002) (contending that regulators should reject strong versions of this principle but take into account "societal aversion to risks of large harm and the value of obtaining additional information") (emphasis omitted).

that in *n*-person variable-sum games, there is no commonly accepted account of rationality, especially if *n* is very large.[151] In fact, the problems at the intersection of welfare economics and game theory go much deeper. It is not merely the so-called Scitovsky paradox—that under some conditions both of two states of a system are Kaldor-Hicks efficient with respect to each other[152]—that is at stake here.[153] It is well known that Scitovstky's substitute criterion for social improvement gives us nothing more than Pareto optimality.[154] Further, in 1974, Robin Boadway argued that in certain cases involving two or more consumers, a Scitovsky-like inconsistency exists under Kaldor-Hicks potential compensation, despite the use of then-existing compensation tests.[155] Moreover, in 1990, Blackorby and Donaldson generalized Boadway's result by showing that whenever the Kaldor-Hicks criterion is inconsistent, so is the compensation-variation metric.[156] Blackorby's generalization might well apply to compensation for injuries caused by stem cell products.

Later work shows that, with some restrictions, a rational equilibrium exists in an *n*-player non-zero sum game where *n* is very large. To illustrate, Peter J. Hammond contends that for each of certain normal-form games, there is a Bayesian rational solution that satisfies all consequentialist axioms.[157]

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[151] *See supra* text accompanying note 117.

[152] T. de Scitovsky, *A Note on Welfare Propositions in Economics*, 9 REV. OF ECON. STUD. 77, 88 (1941) (responding to Nicholas Kaldor, *Welfare Propositions of Economics and Interpersonal Comparisons of Utility*, 49 ECON. J. 549 (1939) and J.R. Hicks, *The Foundations of Welfare Economics*, 49 ECON. J. 696 (1939)).

[153] I say "so-called" paradox because Scitovsky's article just identifies an inconsistency in the foundations of welfare economics, not a logical, semantic, or epistemic paradox.

[154] *See, e.g.*, ALLAN M. FELDMAN, WELFARE ECONOMICS AND SOCIAL CHOICE THEORY 142-45 (1980) (explaining this limitation of Scitovsky's criterion).

[155] Robin W. Boadway, *The Welfare Foundations of Cost-Benefit Analysis*, 84 ECON. J. 926, 932-37 (1974).

[156] Charles Blackorby & David Donaldson, *A Review Article: The Case Against the Use of the Sum of Compensating Variations in Cost-Benefit Analysis*, 23 CAN. J. ECON. 471, 476-80 (1990).

[157] Peter J. Hammond, *Consequentialism and Bayesian Rationality in Normal Form Games, in* GAME THEORY, EXPERIENCE, RATIONALITY: FOUNDATIONS OF THE SOCIAL SCIENCES, ECONOMICS AND ETHICS, IN HONOR OF JOHN C. HARSANYI 187, 191-94 (Werner Leinfellner and Eckehart Köhler eds., 1998). Hammond's demonstration creates an additional player *i** in an *n*-person game such that each *i*-player treats *i** as though he or she faces a single-person normal-form decision tree. Treating the actions of *i** as having occurred prior to the start of this game compresses the original game to a sub-game of

However, his solution requires that the game fall within the family of normal-form decision trees that contain only decision nodes, terminal nodes with corresponding payouts, chance nodes with strictly positive objective probabilities, and a finite set of possible uncertain states of nature, with all probabilities known to all players.[158] Even if Hammond's reasoning is sound, the restrictions on the nature of the game in question are substantial. In addition, his approach is computationally intensive. The likelihood that any real-world person is going to be able to compute his or her subjective utility in regard to stem cell products by these means is virtually nil. It is remarkable that the main treatise on game theory aimed at law professors contains no mention of the literature cited here.[159]

The problems raised by a neoclassical approach to the risk of defective stem cell products and liability for the defective products are now bracingly clear. Debates over rationality and individuals' faulty heuristics and biases reveal the huge "if"-clause contained in unaltered neoclassical approaches: *If* humans were perfectly rational, transactions were costless, and the difficulties with monetization and the application of Coase's theorem were to disappear, *then* we could demonstrate various economic propositions like those endorsed earlier by Geistfeld.[160] That is like saying that if the sky were to fall, we could all catch larks.

V. WHAT THE LAW SHOULD BE ON LIABILITY FOR STEM CELL PRODUCTS

As discussed in Part IV, there are considerable problems with using neoclassical economics to develop an account of liability for stem cell products that works well in the real world with actual human beings. A proposed liability scheme must account for factors that cannot be analyzed in neoclassical economic concerns or sometimes in purely economic terms of any kind. In the following sections, I argue that a qualified regime of strict liability with a partially socialized insurance component can account for these economic and non-economic factors.

In this part, the first section provides the basic arguments for and against strict liability, adjusts these arguments to account for economic and non-

incomplete information. Once *i**'s optimal decision along the decision tree is determined, each original *i*-player should choose the decision set that maximize his or her subjective expected utility based on the subjective probabilities that are appropriate for all decision trees faced by *i**.

[158] *Id*.

[159] BAIRD ET AL., *supra* note 117.

[160] *See supra* text accompanying notes 104-119.

economic factors, and defends the resultant vector of these arguments as a provisional conclusion. Here, I use the metaphor of vectors to analyze the outcome of competing arguments. An argument has a vector if it bears on a factor, that is, if it points towards a particular objective in light of a particular issue or consideration. An argument has more than one vector when it bears on more than one factor. The resultant is the sum of these vector arguments.

The second section elaborates on this conclusion by applying the altered economic analysis to discuss how my proposed liability regime would handle the risks associated with stem cell products.

The third section supplies some details of the qualified strict liability regime. The heart of my proposal consists of a modified strict liability regime for stem cell products that are defective in design or manufacture or have inadequate warnings. The regime's socialized insurance scheme is funded by contributions from manufacturers, patients, and the public fisc. The regime is qualified by six modifications that separate it from a pure strict liability regime: an unavoidably unsafe rule, a learned intermediary rule, FDA approval as a rebuttable presumption, a state-of-the-art defense, a collateral-source rule, and various limitations on damages.

A. The Resultant of Vector Arguments For and Against Strict Liability

The basic argument for strict liability runs as follows: At present, stem cell research is in its infancy. Aside from hematopoietic stem cells, there are very few stem cell products on the market. When non-hematopoietic stem cell products receive FDA approval in large numbers, patients are likely to have little information on the products' risks and benefits. Consider, for example, the use of hESC-derived oligodendroglial precursor cells to replace cells in the spinal cord destroyed by trauma.[161] Even if patients have any information, some of the patients will be unable to evaluate the information critically. In contrast, makers of stem cell products, such as the Geron Corporation in this case,[162] will know much more about the risks and benefits than patients will. Furthermore, manufacturers are in a better position than patients to increase the safety and effectiveness of stem cell products. They are better situated than patients to absorb the costs of harm caused by these products, for they can buy insurance or self-insure against judgments for damages. Moreover, manufacturers know how to instruct physicians in the use of stem cell products better than patients do and can better warn physicians and patients about risks associated with these products. Therefore, those who make stem cell products

[161] *See supra* text accompanying note 15.

[162] *See* Young, *supra* note 15.

should be strictly liable for any harm they cause.

The basic argument against strict liability, and in favor of fault liability, goes like this: For a firm, even a substantial biotechnology company like Geron, receiving FDA approval for any drug, biologic, or combination product is an expensive proposition. Little reason exists to think that it will be less expensive, on average, for a stem cell product classified as a biologic or combination product. In addition, makers of any such product face fault liability, which increases their costs. If their product is negligent in design or manufacture, or if makers negligently fail to warn or to give proper instructions for use of the product, they have to pay damages for harm caused by their negligence. To make them strictly liable for such harm could be undesirable in one or another of several ways. For example, firms could decide not to make stem cell products at all, which could deprive patients of needed therapies. Another possibility is that firms decide to make the products but could raise the price to cover their insurance premiums if insurance is available, or to self-insure with a backup plan to file for bankruptcy if financial liability threatens to destroy the firm, as happened in asbestos litigation. In the former case, the price of hESC-derived oligodendroglial precursor cells would exceed the coverage provided under many health insurance plans or the ability of many patients to pay out-of-pocket, and in the latter case many patients would not be able to recover in full the damages awarded them in court. To impose liability without regard to fault would thus be financially bad for manufacturers or patients or both. In consequence, strict liability for harm caused by stem cell products would not be justifiable as a matter of legal policy.

If one makes adjustments, however, it is possible to take some of the sting out of the argument against strict liability. First, make FDA approval of a firm's oligodendroglial precursor cells a rebuttable presumption of safety and effectiveness. This move does not eliminate strict liability altogether, but it does put a somewhat greater burden on plaintiffs to make a prima facie case and to establish their position by a preponderance of the evidence. Second, introduce a state-of-the-art defense such that a manufacturer need not incorporate into the design of its product a technical advance that appears in later products of the same type.[163] Third, limit damages in one or more of the following ways: impose damage caps, preclude punitive damages, and limit damages for pain and suffering. Fourth, introduce a collateral source rule of the following sort: if a victorious plaintiff harmed by a stem cell product has health insurance coverage that pays for medical and hospital expenses, he or she must relinquish whatever portion, if any, of the damages award that

[163] *See, e.g.*, VISCUSI, *supra* note 119, at 196-97.

reimburses for those expenses. This rule prevents recovery from two different sources for the same item of loss.

The adjustments just mentioned can be challenged on at least a trio of general grounds. One is that the adjustments are likely to be somewhat inefficient, for manufacturers can avoid the costs imposed by defective hESC-derived oligodendroglial precursor cells more easily than patients. Manufacturers are not required to internalize all of their externalities. Another ground is that the adjustments reduce the deterrent effect of unadjusted strict liability. The unadjusted version creates an incentive for manufacturers to make these precursor cells as safe as possible and to exercise caution in drafting warnings and instructions. Still another ground is that the adjustments shift wealth from harmed patients to manufacturers, and this distributional consequence is unwarranted, for as a general matter patients are less well-off than manufacturers.

This trio of ripostes carries some weight, but it does not address the likely claims of manufacturers that unadjusted strict liability for the precursor cells might induce them not to enter the market at all, or to push up dramatically the prices of these products, or to devise bankruptcy mechanisms for deferring the payment of judgments or escaping payment altogether. Thus, anyone who thinks that stem cell products could have value for society should consider socializing the insurance function.

For sake of argument, assume that neither manufacturers alone nor patients alone could insure adequately against harm caused by a firm's oligodendroglial cells derived from hESCs. One might then pursue one or more of several ways of coming up with adequate insurance: (1) require both manufacturers and patients to contribute a certain amount per product to a compensation fund; (2) use the Federal Tort Claims model for stem cell products, as suggested by James M. Wood and colleagues,[164] to make the federal government the insurer; (3) adapt the VICP model, now employed as a no-fault alternative for children's vaccines, to stem cell products, with complete federal preemption of any state laws to the contrary, except for state blood shield laws, which again makes the federal government the insurer. Now (1) is compatible with either (2) or (3). But (2) and (3) are not compatible with each other, for (2) is a tort product liability model and (3) is a no-fault model.

Before drawing a conclusion, I add a further element to the mix: a life-cycle approach to stem cell products. One of the most valuable features of the 2007 Institute of Medicine report on drug safety is its emphasis on the life cycle of a

[164] Wood et al., *supra* note 85, at 12-13.

drug.[165] Stem cell products, like drugs do now, will almost certainly have a natural and legal life cycle that includes research, invention, submission of an application to the FDA, clinical trials for safety and effectiveness, approval, post-market reports on the risks and benefits, and often eventual waning as better products or therapies come along. Throughout this Article I have stressed that few non-hematopoietic stem cell products yet exist. Hence only informed predictions about these products, not hard evidence, are now available. That will not always be so. Over the next several decades we will know much more about these products.

Accordingly, it would be foolish to pronounce, once and for all, on the ideal product liability arrangements for stem cell products. Given the limited information available, one should probably favor a much-modified system of strict liability to start. The basic argument for a pure strict liability regime is vulnerable to criticism, for it might prevent or delay these products coming to market, greatly increase their prices, or not get prompt, adequate recovery to those harmed. A pure system of fault liability is also vulnerable to criticism, because it would preclude compensation for some who are harmed by stem cell products. Still, several fault-liability-inspired adjustments make sense: FDA approval as creating a rebuttable presumption of safety and effectiveness, a state-of-the-art defense, various limitations on damages, and a collateral source rule.

And yet, a strict liability regime with these minor adjustments is open to attack from both sides. Patients can point to inefficiency in the failure to use the cheapest-cost-avoider rule of thumb, reduced deterrence against the manufacture of insufficiently safe and effective stem cell products, and an unwarranted shift of wealth from harmed patients to manufacturers. For their part, manufacturers can point out that, if one thinks stem cell products are socially worthwhile, the minor adjustments do not solve the problem of getting these products to market at a reasonable price and in a timely way with certain, swift, and adequate compensation for injured patients.

The way out of this impasse is to socialize the insurance function. Both the makers of stem cell products and the patients should contribute some amount per product to a compensation fund run by the federal government and otherwise funded from general revenues. Payouts from the fund could proceed under either a federal tort claims model or a no-fault model adapted from that for children's vaccines. The contributions from three sources—manufacturers,

[165] INST. OF MED. OF THE NAT'L ACADEMIES, COMM. ON THE ASSESSMENT OF THE US DRUG SAFETY SYSTEM, THE FUTURE OF DRUG SAFETY: PROMOTING AND PROTECTING THE HEALTH OF THE PUBLIC chs. 1-3 (2007).

patients, and the public fisc—would thus give each an incentive to hold down administrative costs. Over time, as more information becomes available on the risks and benefits of stem cell products, and the advantages and disadvantages of this compensation system, the much-modified strict liability regime that we have sketched, should be reevaluated. Given the life cycle of various stem cell products over the coming decades, others would then be in a good position to decide whether the proposed regime should be retained, scrapped, or revised in ways that no one can now anticipate.

This dramatically modified strict liability system is superior to the system of product liability available under existing law. Current law would provide a more robust system of strict liability, offset only by such features as the unavoidably unsafe rule and the learned intermediary rule, more or less in line with Section 6 of the *Restatement*. This robust system could well inhibit manufacturers' willingness to bring stem cell products to market. Because stem cell technology has great promise, a distinctly modified strict liability regime is provisionally to be favored over other options. An important aspect of this provisional regime lies in its attention to the life cycle of stem cell products. As more information becomes available on these products, the regime should be adjusted accordingly.

The regime just sketched is largely unaffected by the recent dispute between Professors Polinsky and Shavell on the one side and Professors Goldberg and Zipursky on the other on the general case for product liability.[166] The former regard the case as uneasy and the latter see it as easy. In two respects their debate has little impact on my argument. First, Polinsky and Shavell claim that only for widely used products do the costs of product liability exceed its benefits.[167] Stem cell products are not widely used now. Perhaps they will never enjoy such wide use as the examples cited in their article, namely automobiles, airplanes, and vaccines. Second, both market forces and regulatory schemes are capable of increasing safety, Polinsky and Shavell maintain, only when consumers and regulators are aware of the risks.[168] In the

[166] A. Mitchell Polinksy & Steven Shavell, *The Uneasy Case for Product Liability,* 123 HARV. L. REV. 1437 (2010); John C. P. Goldberg & Benjamin C. Zipursky, *The Easy Case for Products Liability Law: A Response to Professors Polinksy and Shavell,* 123 HARV. L. REV. 1919 (2010); A. Mitchell Polinksy & Steven Shavell, *A Skeptical Attitude about Products Liability* Is *Justified: A Reply to Professors Goldberg and Zipursky,* 123 HARV. L. REV. 1949 (2010).

[167] A. Mitchell Polinksy & Steven Shavell, *The Uneasy Case for Product Liability,* 123 HARV. L. REV. 1437, 1474 (2010).

[168] *Id.* at 1443-46.

case of stem cell products, where the risks are unknown, there is a stronger case for placing liability on designers and manufacturers, who are better positioned than consumers to know and discover the risks. Third, in at least one place Goldberg and Zipursky have the better argument: the accountability and evident fairness of a product liability system represents an important advance over purely economic considerations.[169]

B. Triangulation and the Ethics of Risk Imposition

In order for the qualified strict liability regime to work for stem cell products in the real world, it must account for the fact that patients and physicians will commonly use heuristics to make decisions with imperfect information and under bounded rationality. In light of these realities, the goal of this section is to delineate how my proposal will deal with risk. I begin with a discussion of how manufacturers, physicians, and patients may analyze and manage the risk involved with the use of stem cell products.

Because many of the dangers associated with the potential use of stem cell products are unknown, I employ the concept of triangulation to navigate the complexity of risk. The triangulation metaphor comes from a "navigation and military strategy that use[s] multiple reference points to locate an object's exact position."[170] Here, the aim is to structure my proposal to account for the risk of stem cell products, even though that risk itself is hitherto undetermined, by drawing upon economic theory and moral philosophy.[171] I intend my regime to apply to all stem cell products, but recognize that making adjustments in the case of particular products is bound to be necessary.

1. Triangulation: Risk Analysis and Management

If physicians, patients, manufacturers, legislators, and regulators have to decide what to do in ways that fall short of archangelic knowledge and intelligence,[172] it seems likely that they can begin their risk analysis in this

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[169] Goldberg & Zipursky, *supra* note 166, at 1942-48.

[170] Todd D. Jick, *Mixing Qualitative and Quantitative Methods: Triangulation in Action*, 24 ADMIN. SCI. Q. 602, 602 (1979) (discussing the various conceptions and applications of the triangulation metaphor as a social science research paradigm).

[171] As Jick explains, the common thread among all methods involving triangulation is the "search for a logical pattern in mixed-method results . . . [where] the researcher [i]s builder and creator, piecing together many pieces of a complex puzzle into a coherent whole." *Id*. at 608.

[172] For a different purpose, Hare invents an "archangel" who has "superhuman powers of thought, superhuman knowledge and no human weaknesses." R. M. HARE, MORAL

way. The two main risks of stem cell products, such as hESC-derived insulin-producing cells, involve safety and effectiveness. As to safety, physicians and patients, especially, but manufacturers as well, should have accessible information that addresses the likelihood of adverse effects, the severity of these effects, and the timing of the impact of stem cell products that turn out to be effective. Based on such information, physicians and patients can compare stem cell risks with the risks associated with alternative treatments. So far as effectiveness is concerned, they need whenever possible information in straightforward percentage terms that allow for easy comparison. Dealing with effectiveness risk will be easier if the risk is, whenever possible, expressed in terms of percentages, or at least a range of percentages. Tables and charts are highly useful for this purpose. Yet no good comes from making effectiveness risks seem numerically clearer than they actually are. If there is no sound basis for assigning probabilities even within a range, it will mislead patients and physicians to attempt to do so.

For this reason, it is vital that information about the risks of stem cell products be available in an accessible format that lends itself to understandable comparisons. If a given risk affects both safety and effectiveness, it should appear under both headings. Though this practice might seem redundant, it is in fact expedient because it increases the chances that patients and physicians will absorb all relevant information. The best way to ensure that such information becomes available is to require manufacturers of stem cell products to disseminate information about risk within the categories of safety and effectiveness.

Safety has priority over effectiveness in risk analysis. If possible, the FDA and manufacturers should agree that safety risks that are wholly disproportionate to the potential therapeutic benefits of stem cell products are unacceptable. They ought, moreover, to agree that the products in question should not appear on the market—though they might have some nonmarket availability in a compassionate-use program.[173] The FDA and manufacturers should, in regard to acceptable safety risks, present information that clearly identifies the severity of the harm, the probability of its occurrence, and the

THINKING: ITS LEVELS, METHOD, AND POINT 44 (1981).

[173] *See* 21 C.F.R. § 312.320 (2009) (describing "expanded access use" of IND). For a description of when "compassionate use" qualifies for "expanded access use" of IND under FDA regulations, see RESEACH COMPLIANCE OFFICE, STANFORD UNIVERSITY, CLARIFICATION OF FDA REGULATIONS AND GUIDANCE ON "COMPASSIONATE" AND "HUMANITARIAN" USE (2006), *available at* http://humansubjects.stanford.edu/research/documents/compassionate_humanitarian_use_FDA_GUI01036.pdf.

timeline of impact—all to the extent possible under the circumstances. Severity of harm ranges from minor risks of infection or allergic reactions to risks of trauma, chronic disease or disability, and death. The timeline of impact should display the predicted onset of adverse events over time. To illustrate, a stem cell product that involves grave risks in the short term might be acceptable to a terminally ill patient if the severe harm is unlikely to occur until three years have passed. In contrast, a stem cell product that involves many short-term minor risks might be unacceptable to a patient who has a chronic disease for which there are other cures or treatments.

Though the effectiveness of stem cell products almost always will take a back seat to safety, the risk that a particular product will prove ineffective in treating a particular disease or condition might loom large in the decision-making of physicians and patients. If a patient is gravely ill, a high probability of ineffective treatment poses a severe danger, especially if an alternative treatment cannot be used at the same time. Contrariwise, should a patient have a chronic disease that is neither life-threatening nor disabling, a modest risk of ineffective stem cell treatment poses minimal danger. Observe that effectiveness risks and safety risks are sometimes connected in the following way: An ineffective treatment often delays the opportunity to use a more effective therapy that has nothing to do with stem cell products, and thereby creates some safety risk to the patient until the failure of the treatment becomes apparent.

Reducing risk is a vital component of any risk-management program. It is important not to rest, content with safety and effectiveness risks associated with stem cell products, but to seek to lower these risks over time. Here I mark the possible contributions of patients, physicians, and manufacturers. Together, patients and physicians should keep abreast of current research and information. Manufacturers should strive continually to improve the safety and effectiveness of their stem cell products.

Manufacturers of stem cell products thus have to make key judgments about whether a stem cell product is safe and effective enough to seek FDA approval for marketing the product. They also need to have a clear-eyed view of the legal risks in the event that their product proves to be ineffective or, especially, unsafe. Lawmakers and regulators should ensure that all risk information associated with new and existing stem cell products is accessible and presented lucidly. In particular, regulators have to determine acceptable risks of stem cell products like insulin-producing cells derived from hESCs. They must also, like manufacturers such as Novocell, make risk-management decisions regarding the liability of manufacturers for defective stem cell products.

True, not all acceptable risks can feasibly be lowered. If they cannot be,

they count as unavoidable risks. Such risks will lead to some injuries and other adverse events, whose impact on the health and welfare of patients merits careful review. No one should determine lightly that a risk is both unavoidable and acceptable. A mandatory insurance program should perhaps cover cases that, after thorough review, involve a risk that is both unavoidable and acceptable.[174]

2. Ethics of Imposing Risks

This Article takes the ethics of risk imposition seriously. Elsewhere, I have voiced sympathy for Scanlon's approach to risk assessment and risk distribution.[175] Here, I articulate such an approach for the risks imposed by stem cell products and relate it to various "codified" ethics.

According to Scanlon, the soundest ethical principles "are those we are best able to justify to others where, crucially, this justifiability is understood as justifiability to *each other person*."[176] Scanlon's "contractualist" approach thus differs from aggregative approaches such as utilitarianism under which one person may sometimes be justifiably sacrificed to improve the lot of others.[177] An alternative formulation of his approach is that the soundest ethical principles are those to which no one could reasonably reject.[178] An obvious objection to Scanlon's view is that it would lead to paralysis—that is, no principles for the ethics of risk imposition are justifiable, for nary a principle can be found to which at least one person cannot reasonably reject. This objection is mistaken. For example, the principle that ambulance drivers may within limits disregard some traffic laws in urgent situations cannot reasonably be rejected.[179] The risk that a speeding ambulance on the wrong

[174] *See, e.g.,* DAVID A. MOSS, WHEN ALL ELSE FAILS 234-35 (2002) (arguing for such insurance coverage).

[175] *See, e.g.,* THOMAS M. SCANLON, WHAT WE OWE TO EACH OTHER (1998); Stephen R. Munzer, *Human-Nonhuman Chimeras in Embryonic Stem Cell Research,* 21 HARV. J.L. & TECH. 123, 135-36 & 136 n.44 (2007).

[176] James Lenman, *Contractualism and Risk Imposition,* 7 POLITICS, PHILOSOPHY & ECON. 99, 100 (2008) (emphasis in original).

[177] *See* Alastair Norcross, *Comparing Harms: Headaches and Human Lives,* 26 PHIL. & PUB. AFF. 135 (1997); T.M. Scanlon & Jonathan Dancy, *Intention and Permissibility,* 74 PROC. OF THE ARISTOTELIAN SOC'Y 301 (2000).

[178] *E.g.,* Elizabeth Ashford, *The Demandingness of Scanlon's Contractualism,* 113 ETHICS 273, 276 (2003); F. M. Kamm, *Owning, Justifying, and Rejecting,* 111 MIND 323 (2002).

[179] Lenman, *supra* note 176, at 101.

side of the road might injure someone is acceptable because it is possible to justify it to each and every reasonable person.

Scanlon's approach better recognizes the separateness of persons and the duty to treat them as ends rather than means than do various forms of consequentialism.[180] Scanlon's approach is also superior to Rawls's view that the soundest ethical principles are those to which everyone would agree in the original position—that is, would accept from behind a veil of ignorance.[181] Under Scanlon's approach, justification is *ex post*, or so at least it is generally understood.[182] However, there is warrant for thinking that making his approach *ex ante* would be philosophically sounder, because reasons pertaining to risk should be presented to an agent before she chooses.[183] In any case, ethical principles for risk imposition have to be justifiable to the most burdened individual.[184]

In the present context, the payoff of Scanlon's approach is that neither physicians nor FDA employees nor the designers and manufacturers of stem cell products may justifiably impose on patients risks that patients could reasonably reject. The patient is an end in himself or herself and may not be used solely as a means. A competent patient with adequate information can, of course, decide to undergo a risky stem cell treatment. But no one may take advantage of a patient by suppressing relevant information, pressuring a patient to make a hasty decision, or deceiving a patient who is unable to spot the trick. Enhancing one's reputation as a physician, or generating higher profits for a biotechnology firm never justifies treating a patient solely as a means.

The general good sense of Scanlon's approach is discernible in the practical "codified" ethical principles that apply to physicians and others. The American Medical Association ("AMA") has a code of ethics that applies to treating physicians and in some respects to clinical investigators.[185] Some

[180] *See id*.

[181] *See* JOHN RAWLS, A THEORY OF JUSTICE 118-92 (1971).

[182] Lenman, *supra* note 176, at 115-16.

[183] This Article cannot pursue the complexities of *ex ante* versus *ex post* approaches. It bears mention that some philosophers disagree fundamentally with Scanlon's views. *E.g.*, Barbara H. Fried, *Can Contractualism Save Us from Aggregation?,* Stanford Public Law Working Paper No. 1781092 (2011), *available at* http://ssrn.com/abstract=1781092. I have benefited from conversation with Aaron James on these issues.

[184] Lenman, *supra* note 176.

[185] COUNCIL ON ETHICAL AND JUDICIAL AFFAIRS, CODE OF MEDICAL ETHICS OF THE AMERICAN MEDICAL ASSOCIATION, Op. 2.07 (2010-2011), *available at* http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics.shtml (the standards applicable to treating physicians and clinical investigators coincide in some

AMA opinions indicate only which ethical considerations should be taken into account.[186] Others state specific obligations of physicians.[187] A physician must consider whether a treatment is necessary and beneficial to the patient.[188] He or she must also secure informed consent.[189]

Other professional associations have codes of ethics. In the case of designers and manufacturers of stem cell products, however, it is harder to find professional principles pertaining to risk and to be sure that they guide behavior. For this reason, the adoption of Scanlon's perspective on the ethics of risk imposition could yield practical benefits.

C. Some Details of the Product Liability Proposal

1. Aims of the Qualified Strict Liability Regime

Because of the cellular nature of most anticipated stem cell products, it may be difficult to judge whether any harm appearing after the product's use resulted from the provider administering treatment, from the designer or manufacturer of the product, from some other party along the production chain, or from a cause that has nothing to do with the product. Even if one rules out an extraneous cause, it may hard to distinguish between defective design and defective manufacturing on the one hand, and to distinguish between product liability and medical malpractice issues on the other. To see how a qualified strict liability regime for stem cell products would work, it helps to map out some salient liability-suit scenarios and to consider collective and proportional liability theories.

(a) Liability-Suit Scenarios. Lawsuits involving stem cell products are apt to fall into three main classes: defective design suits, defective manufacturing suits, and inadequate warning suits.[190] To craft a liability regime, notice that

places).

[186] *E.g.*, *id.* Op. 2.078 – Guideline to Prevent Malevolent Use of Biomedical Research.

[187] *E.g.*, *id.* Op. 2.067 – Torture ("Physicians must oppose and must not participate in torture for any reason.").

[188] *Id.* Op. 8.06 – Prescribing and Dispensing Drugs and Devices.

[189] *Id.* Op. 8.08 – Informed Consent ("The physician's obligation is to present the medical facts accurately to the patient or to the individual responsible for the patient's care and to make recommendations for management in accordance with good medical practice. The physician has an ethical obligation to help the patient make choices from among the therapeutic alternatives consistent with good medical practice.").

[190] Tomas J. Philipson & Eric Sun, *Is the Food and Drug Administration Safe and Effective?*, 22 J. ECON. PERSP. 85, 90 (2008).

defective manufacturing and inadequate warning suits[191] are more common for drugs, whereas defective design suits are more common for medical devices.[192] Lawsuits involving stem cell products that fall into one or more of these classes are likely to pose different challenges and issues.[193]

Detecting design flaws is already difficult. The difficulty may increase in the case of stem cell products as compared with drugs. Such products are new and likely to have a device component. Because designers are apt to protect their patents or other proprietary rights, they will not give up their design secrets readily. Further, there is always the problem of showing whether an alternative safer design existed at the time the product was made. No hope exists of eliminating this problem, but there is a very pressing hope of reducing its severity. One way to do so is by making a state-of-the-art defense available to designers. It is, by comparison, less pressing to ensure that manufacturers can assert this defense.

Different considerations apply to inadequate warning suits. These suits typically involve an alleged failure to provide enough information about a product and the risks of using it.[194] The typical response is a call for more information from the designer or manufacturer. If the call is heeded, physicians and patients benefit from the transparency. One fly in the ointment is that disclosing more information can lead to greater tort exposure for designers and manufacturers. A second fly is that greater tort exposure can lead designers and manufacturers to reduce voluntary activities that might create negative information, which in turn can lead to less information than would have been available without the call for more information. For instance, a firm might conduct a post-market study that reveals negative outcomes that confirm, only in retrospect, a problem weakly suggested by earlier evidence. This confirmation might well lead firms to cease post-market clinical trials.

The second fly in the ointment, sometimes misleadingly called the "transparency paradox,"[195] has to do with the predictable backfiring of some changes in the rules of tort and administrative law. Whatever one calls this phenomenon, my qualified strict liability regime would respond to it by

[191] I use "inadequate warning suits" to cover also lawsuits involving an utter failure to warn.

[192] Philipson & Sun, *supra* note 190, at 91.

[193] *Id*. at 91.

[194] *Id*.

[195] Daniel R. Cahoy, *Medical Product Information Incentives and the Transparency Paradox*, 82 IND. L.J. 623 (2007). In my judgment, this backfiring is not a paradox at all, only a predictable result of rejiggering the rules of tort and administrative law.

limiting the sorts of information that plaintiffs can use in inadequate-warning stem cell product liability lawsuits. To illustrate, pharmaceutical firms sometimes conduct post-market studies to determine whether, and if so, how, certain drugs perform differently within racial groups. If one thinks that information of this sort would be useful in the case of stem cell products, one should limit plaintiffs' use of this information in court. Differently, because it makes sense to provide an incentive for early disclosure of information on the safety and effectiveness of stem cell products, one might reward early disclosure by limiting its use in court while giving no special treatment to late or delayed disclosure.

Lastly, in this survey of liability-suit scenarios, one should address the scope of an FDA-approval rebuttable presumption of safety and effectiveness and potential limits on damages. As to a presumption, it appears justifiable to limit its scope to defective design suits. Manufacturers ought not to be included, for FDA approval should not extend to poorly made stem cell products. Neither should inadequate warnings be included, because FDA approval is predicated on adequate information and warnings. It may be that a rebuttable presumption based on FDA approval might have greater scope *in the future*. If and when the risks of stem cell products become more predictable and the FDA gains more experience in *effectively* regulating these products, then that may warrant more protection for manufacturers that have met all FDA requirements.

In response to the potential criticism that my product liability proposal is too tough on designers and manufacturers, one might consider some limits on punitive damages. True, product liability for damages of all kinds is generally a matter of state law. But occasionally the federal courts have placed limits on punitive damages.[196] I would not, however, favor limits on punitive damages for stem cell products until the following conditions are met. First, designers and manufacturers have received FDA approval. Second, they have fully complied with all FDA regulatory requirements. Third, the risks of stem cell products have become more predictable. And fourth, the FDA has gained experience in effectively regulating these products.

(b) Collective and/or Proportional Liability Theories. These theories are worth considering in situations where it is difficult or impossible to identify which firm or firms designed or manufactured the stem cell product, to decide which firm or firms caused the harm, and to determine, if multiple firms and

[196] *See, e.g.*, State Farm Mut. Auto. Ins. Co. v. Campbell, 538 U.S. 408 (2003) (holding that the due process clause usually limits punitive damages to less than ten times the compensatory damages awarded).

individuals are involved, the degree to which each firm caused the harm at issue. The legal system ought to use theories of this sort sparingly.[197] Yet one can readily imagine a case in which a stem cell product harms a patient where one firm developed a hESC line, other firms turned it into a final product, and it is hard or impossible to determine which firm caused the harm. Here it might be appropriate to employ market-share liability or some other form of shared or proportional liability.

2. A Socialized Insurance Function

The public fisc bears responsibility for stem cell product liability as an insurer of last resort. Yet before any government responsibility kicks in, liability rests on contributions from firms and patients. Some discussion is in order to show how these contributions might be determined.

As to firms, the most obvious way is paying a certain amount per product into a compensation fund. A less obvious alternative, or additional, way is paying a certain amount based on its market share—of either all stem cell products or of stem cell products of the sort the firm makes. A significant criticism of market share liability, however, is that it can create a free-rider problem if some firms meet or exceed standards of safety and effectiveness. These firms in effect subsidize competitors that have lower standards, which could lead to a reduction in incentives for all firms to design and make safe stem cell products.

Nevertheless, one can minimize this problem by taking additional factors into account. These include a firm's efforts to improve safety and effectiveness, the success of its efforts, its securing of FDA approval, and its compliance with post-market regulations. A firm's contribution should go down to the extent that it ranks highly in one or more of these respects. It should go up if it ranks low. Allen Rostron, for example, recommends

[197] In fact, our legal system does not often use them. For instance, since the market-share liability ("MSL") theory was first employed in the diethylstilbestrol cases, most courts have shied away from MSL on the ground that for most products the fungibililty requirement is unmet. Allen Rostron, *Beyond Market Share Liability: A Theory of Proportional Share Liability for Nonfungible Products*, 52 UCLA L. REV. 151, 170-73 (2004). Fungibility requires both qualitative physical indistinguishability and uniformity of risk. *Id*. at 163-67. However, some courts have applied some form of MSL to blood clotting proteins. For instance, in *Smith v. Cutter Biological, Inc*., 823 P.2d 717, 729 (Haw. 1991), the court held that MSL was an appropriate theory to apply when the plaintiff contracted HIV from a contaminated Factor VIII blood product if the plaintiff was unable to identify the specific firm(s) responsible for his harm. For more on the *Cutter* case, see *supra* text accompanying notes 59-62.

supplementing market share data with "product test data . . . to take into account the relative risk posed by each product" and obtaining "expert . . . assessments of the relative risk of each product."[198] The same calculus can be used for stem cell products that carry inherently higher risks associated with their use. For example, once the relative risk of using a particular stem cell product is apparent, producers of higher-risk stem cell products will have to contribute more to the fund.

3. Compassionate Use, Informed Consent, and Patient Preferences

My product liability proposal is receptive to an enlarged role for compassionate use. Of course, many stem cell products might not save lives. They might eventually provide, say, better treatments for chronic diseases for which there are already good treatments. But only a few, at least in the immediate future, are likely to be life-savers. In connection with cancer drugs, Richard Epstein makes the valuable point that FDA compassionate-use exemptions are exceedingly difficult to obtain. The main reason, in his view, is that the FDA "impose[s] all sorts of preconditions which [can] take months or years to satisfy."[199] The delays frustrate patients and lead to unnecessary patient mortality and morbidity. To overcome such nit-picking by the FDA and reduce long delays, Epstein advocates allowing patients to make cancer treatment decisions uninhibited by the FDA under standard "principles of full disclosure and informed consent" because these principles respect "subjective preferences on questions concerning the quality of life."[200] By parity of reasoning, one might in theory argue for extending compassionate use of stem cell products to patients who have a serious or life-threatening condition that has no existing effective treatments.

This argument has practical as well as theoretical weight. But one should bear in mind the differences between cancer drugs and stem cell products. Many cancer drugs have serious known risks, are fraught with unpleasant and sometimes fatal side effects, and are sometimes effective only for a known narrow class of cancers. In contrast, the risks of stem cell products are poorly understood, their side effects are generally unknown, and the products may have a broad range of potential uses. So it is not clear that even Epstein would wish to transfer his basic argument from cancer drugs to stem cell products.

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[198] Rostron, *supra* note 197, at 174.

[199] Richard A. Epstein, *Against Permititis: Why Voluntary Organizations Should Regulate the Use of Cancer Drugs*, 94 MINN. L. REV. 1, 17-18 (2009). For reservations about other aspects of Epstein's article, see *infra* note 201.

[200] *Id.* at 38.

For my part, I mark out only a case for an enlarged compassionate-use program once the risks and benefits of stem cell products are better understood.[201]

VI. RETROSPECT AND PROSPECT

This Article tackles problems that are on or just beyond the horizon. The product liability claims regarding stem cell products will require the most exacting attention to their safety and effectiveness that is possible without imposing an undue burden on manufacturers. Alas, no existing category—whether vaccines or blood products or combination products—offers a perfect legal model for stem cell products. However, one can tease out pertinent features of these categories of tort litigation to show what might work well for stem cell products. Definitive recommendations must wait for these products to appear on the market and for their risks and rewards to become better understood over the coming decades.

This Article cannot tie off all loose ends and rebut every objection. Instead, it is an invitation to the future. Stem cell research does not currently give us a dazzling array of new products. It is a harbinger of things to come.

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[201] I am less sympathetic to Epstein's pervasive emphasis on the supposed rights of patients to make autonomous choices based on their subjective preferences. Too often patients who are in the grip of stress and fear misjudge risks and use faulty heuristics. *See supra* text accompanying notes 134-137, 149, 160. As Shaw once wrote,

> You may on academic grounds allow a child to snatch glowing coals from the fire once. You will not do it twice. The risks of liberty we let everyone take; but the risks of ignorance and self-helplessness are another matter. Not only children but adults need protection from them. At present adults are often exposed to risks . . . beyond their comprehension or powers of resistance or foresight . . . .

GEORGE BERNARD SHAW, PREFACES BY BERNARD SHAW 68 (1938). As before, Epstein might wish to confine his argument to cancer drugs, whose risks and side effects are fairly well known, and not extend it to stem cell products, where that is manifestly untrue. *See, e.g.*, ABELOFF'S CLINICAL ONCOLOGY 459-81 (Martin D. Abeloff et al. eds., 4th ed. 2008), *cited by* Epstein, *supra* note 199, at 10 n.26.