EXAMINING THE NUFFIELD LADDER

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The practice of recognizing and saluting donors for their commitment to plasma donation—compensating them—is growing in importance. This is partly due to a burgeoning global awareness of the importance of treating rare diseases for which plasma protein therapies (PPTs) are developed and administered. Coupled with this increased awareness is a rise in diagnoses, which leads to an increase in the need for treatment. Inevitably, this has led to a greater need for plasma.

With increasing regularity, the work of the Nuffield Council is cited as foundation for justifying self-sufficiency policies that rule out compensation. The Nuffield Council is a UK-based independent think tank, supported by large foundations, which issues opinions on areas of biomedical interest and research, ranging from elder care to emerging technologies. Their work includes analysis of the balance between economic forces and medicinal products of human origin. With Nuffield, the analyses typically arise in the form of questions related to organ donation, medical research, and related fields. Nuffield's work is usually regarded favorably in many different countries and contexts, and must be taken seriously by anyone involved in the many sectors that attract Nuffield's interest.

Through the publication of the CreativCeutical report in 2015, the Nuffield Council's 2012 publication, "Human Bodies: Donation for Medicine and Research" gained greater recognition. The CreativCeutical authors focused on a small portion of a very lengthy and complex Nuffield document which contained considerations from widely disparate and distributed industries and practices throughout all of the health care industry.

The 2012 Nuffield work is not the first generated by that organization focusing on ethical aspects of donation. Nuffield first grappled with these issues more than twenty years ago, in its 1995 report, "Human Tissue: Ethical and Legal Issues." The terms of reference for the 1995 work include recognition of the changing landscape of legal-ethical issues given advancements in basic medical research and technological change. The paper was written in the midst of crises involving variant Creutzfeldt-Jakob disease (vCJD) and property rights in genetic material. Blood and plasma were included as a part of Nuffield's analysis. Importantly, the Council in 2012 noted a critical distinction—and noted that the distinction was even wider than twenty years prior—between transfusible components and fractionated products. It specifically noted that blood donations for transfusion and blood products derived from plasma have compelling differences in safety profile and usage, which have *nothing to do with compensation*. The report states that, for products such as PPTs, "quality and safety *are assured* not only by selection and screening of source materials, but also by the choice and control of manufacturing process." (12.27.2, emphasis added).

This is a highly important notation because, even in the middle of the 1990s, PPTs derived from a well-regulated process were seen as safe and efficacious. Since the 1990's, technology and safety have only improved, and the resulting products have become even safer. Even more to the point, this statement was made as a direct discussion of safety, during the peak of concern regarding vCJD in the United Kingdom. The most obvious point of importance is a glaring omission: that the practice of compensating the donor is not even mentioned.

The 1995 report also highlights the importance of transparency with regard to the procurement of donations; that is, a donor should have the knowledge of the disposition of his or her donation. This comports well with some of the more current thinking on the topic relating to informed consent. It recognizes the ethical considerations regarding how and why an individual decides to spend time and resources in supporting an activity, be it plasma donation, charitable contributions, or others. (James Stacey Taylor, The Source, spring 2014)

The second relevant Nuffield paper is the 2010 Consultation Paper, "Give and Take? Human bodies in Medicine and Research." This document helpfully notes that the term "donor" can be used, "whether or not [the donor] receive[s] *any form of compensation for doing so*." (31, emphasis added). The Nuffield Council also defines "volunteer" with the same proviso—compensation is irrelevant to the cast and definition of the term. Nuffield put the 2010 paper out in an effort to gain insight from interested parties. They cast their net quite wide, examining human clinical trials, cell and tissue donations, transplant policy, blood, donations to science and so on. The bulk of Nuffield's 2010 considerations focused on issues of autonomy,

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legal control, and property rights. Importantly, for the very specific context of the plasma collection industry, little was said about plasma per se and much of the same definitions from 1995 prevailed—acknowledgment of controversy with awareness of practical considerations given the different contexts around the uses of materials of human-origin.

In returning to present day considerations, the Council published its most recent and largest of the reviews, mentioned above, in 2012. This report was initially focused on the UK environment, and one must read, at the very beginning of the document, Nuffield's own cautionary words in interpretation: "Time and again, the report comments on how concepts in this area of donation and volunteering are understood in different ways, at different times, in different circumstances, and by different people...*What works in one context need not work in others*." (p. viii, emphasis added). The authors of the paper therefore recognized the temptation to interpolate one's own political goals atop the analysis contained in this lengthy and complex document. They also recognized the importance of nuance of interpretation in the face of ethical and conceptual complexity.

Much of the today's discussion involving donor compensation policies today, such as that in the CreativCeutical report, focuses on the Nuffield's thoughts on compensating donors for plasma focused on the so-called "Intervention Ladder," presenting a model which seeks to define guidance and encouragement for policymakers considering strictures involving donation of human-derived medicinal products. Of the six rungs on the ladder, the Council notes that the first four (such as raising awareness and encouraging donation) would be considered "altruist."

The Council recommends greater scrutiny on non-altruist "rungs" on the ladder, but does not contemplate a blanket prohibition. Instead, with regard to UK policy, the Council explicitly states that: "Where payment is currently made to such [plasma] donors, the same concerns . . . should be considered... In the case of plasma, for example, given the importance of the need for plasma, the difficulties in sourcing it at present in the UK because of the theoretical risk posed by vCJD, and the highly regulated nature of the donor recruitment and quality systems, it would seem likely that those tests [passing concerns regarding donor treatment] would be met, *and hence that reward for donors in these circumstances would constitute an ethically vindicated rung 6 of our Intervention Ladder*." (p. 196, emphasis added). Again, while Nuffield focuses on the UK, their analysis also makes apparent their own expectation that other contexts could also agree with theirs.

Adapting models to fit different circumstances does present novel solutions to intractable problems; the downside is that forcing a fit from one model may cause greater problems. It seems clear that many of those who would proscribe donor compensation would forget Nuffield's own nuanced view. It is indeed interesting that Nuffield expressly used the compensated donation of plasma as an example of an ethically suitable practice. While Nuffield focused on the UK environment (and noted the UK's dependence on United States plasma for further manufacture), the distinct nature of plasma was called out for mention; specifically, the safety processes used in manufacture, and the special situation of patients dependent on PPTs. Using the Nuffield work to examine these issues is of great utility. It is also crucial to understand the spirit of the Nuffield paper; this helps us recognize what the Council itself has said...especially when it applies to our industry and PPT patients.

In the final count, the Nuffield Council's work points a clear path toward the acceptable ethical construct that our industry uses. The Council's report contemplates the finished products, the needs of the patients, and the importance of donor safety and quality systems, among many other factors. While the document itself acknowledges the complexity of the area of medical products of human origin and much of its language is rightly cautious, the fact that our industry and its practices were singled out for identification as an ethical path is something that reminds the industry of the rightness of our mission. It will also give greater hope to patients around the world that more regulatory and health care systems will see their way to Nuffield's conclusions and create structures in which donors are recognized and patients are fully treated. •