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VALUATION OF THE BENEFITS OF RISK-FREE BLOOD

Willingness to Pay for Hemoglobin Solutions

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Abstract

The dream of artificial blood has existed since the 1960s. Disease-free hemoglobin solutions will be commercially available in 1991. A willingness-to-pay (WTP) survey was undertaken to assess the tangible and intangible benefits to the public from this new product. The positive results suggest that third-party payers should cover this benefit and assist the diffusion of this new technology. From the perspective of industrial marketing, results suggest that there will be little consumer price resistance for hemoglobin solutions within the suggested price range of $225–300 per unit. Management implications of this new product are discussed.

In the 1980s, the quality of blood products, especially the issue of their freedom from disease, created both stress and an opportunity to develop and market new, safer products and services. Hemoglobin solutions represent one such major new product coming to the market in the 1990s. Purified stroma-free hemoglobin solutions were developed in the late 1980s, thanks to scientific advances in polymerization, cross-linking technology, and purification/separation technologies. Risk-free hemoglobin solutions can be made from: (a) human red cells as starting material, (b) bovine red cells (if the public and the physician community would accept such a product), and *perhaps* (c) recombinant DNA-derived hemoglobin.

According to the three companies that are planning to market hemoglobin solutions in 1991, the expected U.S. market demand should increase from 150,000–165,000 units available in 1992 to 3–4 million units available in 1998. If the U.S. demand for transfusions continues to grow at 1.0% per year, 13 million units will be needed in 1993 and 13.7 million units in 1998 (net demand after shunting outdated blood to manufacturers for the production of hemoglobin solutions). Hemoglobin solutions are not a perfect substitute for red blood cells, but they offer several desirable product characteristics: prolonged biologic half-life, oxygen binding/dissociation similar to red cells, no toxic or immunologic side effects, and stability when stored at room temperature for up to 200 days. This last characteristic is interesting because the product can sit in an emergency department vehicle or shelf for months at room temperature. The

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new product may be expensive, but it reduces the cost of storage and handling, and may prove to be quality enhancing.

One small study of 11 patients undergoing elective angioplasty to a single coronary lesion outlined the risk-benefit trade-offs (12). Risks associated with angioplasty can be reduced by use of an autoperfusion balloon catheter that allows passive myocardial perfusion during inflation through a central lumen and multiple side holes in the shaft proximal and distal to the balloon. Sending hemoglobin solution past the balloon reduces the risk of tissue damage and ischemic symptoms during the angioplasty, thus allowing for more prolonged periods of balloon inflation.

EMERGING NEED FOR STROMA-FREE BLOOD

In the landmark decision *Kozup v. Georgetown University* (9), blood banks and hospitals were insulated from liability for unforeseeable risks of infection from contaminated blood products. The court granted a motion for summary judgment in favor of the hospital and the Red Cross because the administered blood in question was the safest product possible based on medical science at the time. As the accuracy of screening tests has improved, the Red Cross and individual hospitals have been held to a higher standard of care. The introduction of hemoglobin solutions in 1991 will further shift the definition of the standard of care (15).

A number of recent studies have identified a high degree of public anxiety regarding transmissible disease in the national blood supply (1;16). The public is concerned with cutting (or eliminating entirely) the risk of infection from homologous transfusions: there remains a 1:100 risk per unit of non-A non-B hepatitis, a 1:250 risk of hepatitis B, a 1:500 risk of human T-cell leukemia virus, and a 1:100,000 risk of human immunodeficiency virus. Individuals' valuations of the risk of infection are dependent upon the nature of the infection, that is, the way of dying from a transfusion-based infection is important in addition to the estimated chance of becoming infected (7). Corporations in the United States are concerned with containing the cost of health care by means of containing risks (2).

The process of manufacturing hemoglobin solutions from human (or bovine) blood involves the isolation and purification of hemoglobin from red cells, then reacting the solution with chemicals to alter its oxygen-binding affinity. The resulting heated sterile solution is free of disease and stable (does not dissociate into subunits).

A number of firms are entering the market for hemoglobin solutions, including the Japanese pharmaceutical company Ajinomoto, in collaboration with the blood banking supplier Fujirebio, and the smaller Canadian company Hemosol. Entrepreneurs in this field have two basic concerns. The first is whether profits from solutions derived from human red cells, which use two units of human cells for each unit of hemoglobin solution produced, will prove sufficient in the face of possible competition in 7–15 years from two substitute products, engineered recombinant-DNA hemoglobin and nonhuman (bovine) hemoglobin solutions. Production of human hemoglobin solutions will involve $110–120 per unit of direct expense, and an estimated $40–60 of marketing and distribution expense. Baxter Healthcare, Northfield Labs, and Biopure are targeting a 50% profit margin for this new product, although governmental and other third-party payers will try to contain such profit margins.

Irrespective of this strategic issue, their second concern is whether informed consumers will value the product more than (or equal to) the suggested retail price. This is a critical question for predicting the speed of technological diffusion (16), which can be answered by the economic technique of placing a value on benefits according to consumers' willingness to pay. Hemoglobin solutions might experience a pattern of growth similar to that of intraoperative autologous transfusion (IAT) programs during the period of 1985–1990 if they were priced as high as $500–600 per unit. With both hemoglobin solutions and IAT blood, the patient avoids the risks of receiving homologous transfusion. Yet IAT has remained a virtual (slow-growing) market rather than strong-growth market, because there is substantial consumer resistance at the current price of $500–600 per unit.

Payers and consumer groups need a valuation of how much the public would pay for a unit of hemoglobin solution. A valuation based on willingness to pay in hypothetical situations is a more egalitarian method than one based on ability to pay as a means of estimating cost–benefit. Ability to pay would undervalue the benefits of health programs because the poor and infirm have less ability to demonstrate the worth of health services with cash.

WILLINGNESS-TO-PAY SURVEYS

The probabilistic nature of a willingness-to-pay (WTP) survey (1:1,000 chance of being a patient in one of the hypothetical scenarios) is necessary in planning any health benefits plan or public service (3;10). Financing decisions must be made in advance, before it is known which members of the group have a chance of developing a new disease. Surveying the generosity of 1,000 people to avoid a 0.001 risk of death the following year, the resulting sum total represents the group's willingness to pay to save one statistical life, which will not be identified until the following year.

It is impossible to plan a rational public service on the basis of the preferences of respondents already undergoing a catastrophe. This problem is described by the von Beumann–Morganstern game theory axiom that a person should pay more per unit of risk reduction, the higher the absolute level of risk (3;13). Most people would be willing to pay more to reduce the risk of death from 99% to 98% than for an equal percentage point reduction from 3.0% to 2.0%. If a gun with 100 chambers were 100% loaded, in a game of Russian roulette, most people would be willing to pay the most to take out the first bullet. However, in the case of a gun with 999 empty chambers and only one bullet, most people would pay an *extra* risk reduction premium to achieve zero risk (4), paying more to cut the risk from 0.001 to 0.0 than to cut it from 0.002 to 0.001.

Since President Reagan signed Executive Order 12291, which called for review of all federal programs and widespread deregulation, managers have been formally valuing the benefits of specific programs and regulations that reduce the risk of death (6). Regulators and insurance executives make decisions based on probability estimates. If the average group member would pay $1,000 to avoid a 0.001 risk of death in 1992, then the group acts as if the value of life equalled $1.0 million (or $1,000/0.001), However, estimates in such surveys include intangible benefits such as the reduction of pain, freedom from worry, and time saved, as well as the simple reduction of mortality.

Some bias exists in any WTP survey. For example, heterosexual nondrinkers express a lower willingness to pay for avoiding a relatively higher and familiar risk, such as an automobile fatality, than a lower but unfamiliar risk, such as dying from AIDS or dying in a nuclear power plant meltdown. However, just because the public's willingness to pay to avoid uncertain risks is not in direct proportion, the nature and seriousness of the risk does not mean that the public's preferences should be ignored. Willingness to pay is less biased than the old traditional alternative of discounted future earnings (13). WTP methods are not biased against the old, the handicapped, the AIDS sufferer, or any particular racial group. The discounted-future-earnings approach runs counter to the emerging ethic that "health care is a right," not just a luxury good consumed in proportion to the patient's ability to pay cash for better care.

A WTP survey was undertaken to assess the tangible and intangible benefits to the public from hemoglobin solutions. An informed population of 20 regional blood bank managers and 50 health services administration students was surveyed in 1990. The study was intended to offer insight into two basic questions. First, there is the question of coverage: Should third-party payers cover this benefit, paying for hemoglobin solutions at triple the price of packaged red blood cells, and so assist the diffusion of this new technology? Second is the issue of industrial marketing: Will there be consumer price resistance to hemoglobin solutions within the suggested price range of $225–300 per unit?

WTP Questions and Answers

Five hypothetical patient scenarios were presented to the subject group of 20 regional blood bank managers and 50 health services administration graduate students. The five services were shuffled and presented in random order, so as not to bias the responses (e.g., scenario one was presented first 20% of the time).

The five scenarios can be summarized as follows:

Scenario One. An elective surgery patient with no previous history of transfusions has deposited 2 units of her autologous blood for use during surgery (because of her fear of getting AIDS). Bleeding is excessive, so 2 units of homologous red cells are transfused along with autologous blood. *Situation with hemoglobin solutions*: 2 units of solution can be administered during surgery. Net risk reduction: 2 units (from 2 to 0 units of homologous blood being used).

Scenario Two. A helicopter ambulance arrives to transport an auto accident victim, bleeding profusely from a crushed leg, to the nearest shock-trauma center. The patient is stabilized and receives 4 units of homologous red cells. *Situation with hemoglobin solutions*: the patient would receive 2 units of hemoglobin solution in the helicopter and a total of only 2 units of homologous blood at the trauma center. Net risk reduction: 2 units (risk reduced from 4 units to 2).

Scenario Three. An emergency department (ED) patient vomits a large volume of bright red blood. The blood bank is called, but compatibility testing is not complete. The only option is to infuse 6 units of uncrossmatched O-negative blood, risking a delayed transfusion reaction. *Situation with hemoglobin solutions*: with an adequate supply of solution on the ED shelf, ready to use without any crossmatching, 6 units of solution will sustain the patient's oxygen transport needs for a few hours. The patient ends up receiving only 3 units of homologous blood components (rather than 9 units). Net risk reduction: 6 units (risk reduced from 9 units to 3).

Scenario Four. A patient has been admitted for life-saving liver transplant surgery. The patient requires 20 units of homologous blood products. *Situation with hemoglobin solutions*: the first 10 units of red cells can be substituted by an equivalent concentration of solution. Net risk reduction: 10 units (risks reduced from 20 to 10 units of homologous red cells).

Scenario Five. During a balloon angioplasty, a very sick patient has a balloon inserted in the coronary artery and inflated to open the occlusion. No provision is made to supply oxygen to tissue distal to the balloon during the procedure, so the probability of a fatal heart attack is 2.0%. *Situation with hemoglobin solutions*: during the procedure, the solution is perfused through the balloon to deliver oxygen to the

Table 1. Imputed Willingness to Pay (WTP) for Valuation of a Unit of Risk-free Hemoglobin Solution and the Value of a Statistical Life Saved (Scenario 5)

Scenarios	In dollars: Median	Tails of the distribution: 10th percentile	90th percentile
S_1 Risk reduction to avoid 2 units of risk[a] (2 cut to 0)	\$4 (2,000)[b]	\$2 (1,000)	\$10 (5,000)
S_2 Risk reduction to avoid 2 units of risk (4 cut to 2)	\$2 (1,000)	0 0	\$4 (2,000)
S_3 Risk reduction to avoid 6 units of risk (9 cut to 3)	\$5 (833)	\$2 (333)	\$10 (1,666)
S_4 Risk reduction to avoid 10 units of risk (20 cut to 10)	\$1 (100)	0 0	\$5 (250)
S_5 Reducing the risk of death from a required procedure from 3.0% to 1.5% with respondent given a 1:1000 chance of being this patient	\$100	\$5	\$200
Implicit value of life in S_5	\$6.6 million	\$330,000	\$13.2 million

Sample n = 20 blood distribution managers, mean age = 52.
[a] A unit of risk equals the risk of one unit of homologous blood, which in 1990, according to the American Red Cross had a 1:100,000 chance of human immunodeficiency virus, a 1:5,000 chance of human T-cell leukemia virus, a 1:250 chance of hepatitis B and a 1:100 chance of non-A non-B hepatitis.
[b] Dollar value per unit in percentages.

cardiac tissue distal to the balloon, thus cutting the risk of death for this very sick individual to 1.5%. Net risk reduction: 1.5% (from 3.0% to 1.5%). (Note: this is an example of hemoglobin solution's offering a potentially improved procedure. However, for the bulk of less severely ill patients with coronary artery disease, the risk reduction from hemoglobin solution perfusion might be less significant, e.g., cutting the risk of fatal heart attacks from 0.21% to 0.19%, and cutting the risk of nonfatal heart attacks from 2.5% to 2.45% – but the patient in scenario five is very sick.)

Each respondent was presented with these five scenarios and asked to consider a situation in which they have a 1:1000 chance of being that patient next year. The question is how much they are willing to pay to have hemoglobin solutions available, reducing their level of risk (scenario 2, 3, 4, 5), or eliminating their risk (scenario 1).

If we compare the responses to scenario 1 and 2 (Table 1), cutting risk by two units (from 2 to 0 units vs. from 4 to 2 units), blood bank managers rationally attach a premium to the elimination of risk. That premium equals \$1,000 for the median respondent, \$2,000 in question two *minus* \$1,000 in question four. However, there is a point where risk is so high that the measured marginal benefit from risk reduction offers only \$100 of benefit (median response), cutting units of risk from 20 to 10 units of homologous blood in question four. This plateau of diminishing benefit, or diminishing WTP, is apparent in the declining median values for both samples (Tables 1, 2).

The students' responses in Table 2 confirm two previous findings (3;4) that young graduate students have WTP responses that are slightly lower than managers over the age of 40. One could speculate that blood bank managers are more educated in risk

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Table 2. Imputed Willingness to Pay (WTP) for Valuation of a Unit of Risk-free Hemoglobin Solution and the Value of a Statistical Life Saved (Scenario 5)

	In dollars		
		Tails of the distribution	
Scenarios	Median	10th percentile	90th percentile
S_1 Risk reduction to avoid 2 units of risk (2 cut to 0)	\$3 (1,500)[a]	\$1 (500)	\$8 (4,000)
S_2 Risk reduction to avoid 2 units of risk (4 cut to 2)	\$2 (1,000)	\$1 (500)	\$3 (1,500)
S_3 Risk reduction to avoid 6 units of risk (9 cut to 3)	\$4 (666)	\$1 (167)	\$7 (1,167)
S_4 Risk reduction to avoid 10 units of risk (20 cut to 10)	\$1 (100)	\$0.5 (50)	\$5 (250)
S_5 Reducing the risk of death from a required procedure from 3.0% to 1.5% with respondent given a 1:1000 chance of being this patient	\$40	\$5	\$70
Implicit value of life in S_5	\$2.64 million	\$330,000	\$4.62 million

Sample n = 50 health administration students, mean age = 27.
[a] Dollar value per unit in parentheses.

assessment and are also older and, therefore, more subject to risk and more in touch with their mortality.

To this point, the analysis has focused on the median individual, the 50th percentile. Subgroups, however, should also be considered. Judging by the results in Table 1 for the 10th percentile, the least risk-averse older managers are most likely to admit a point of diminishing returns and scarce resources and, thus, report a WTP value of zero under scenarios 2 and 4.

Irrespective of the reasons underlying the responses, the important finding is that people in their 20s and 50s exhibit a willingness to pay for a new product that is in excess of the minimum price needed by the manufacturer to make a target level of $100 profit.

The results for scenario 5 reported in Table 1 indicated a median value of a life of $6.6 million in 1990 dollars, a figure consistent with a number of recent studies. For example, one study of occupational WTP (willingness to rake a riskier job in exchange for higher wages), reports a value ranging from $5.2 to 6.5 million in 1986 dollars (11).

HEALTH SECTOR IMPLICATIONS

Hospital managers might consider diversification into the business of hemoglobin solutions. Hospitals can sell raw material (outdated red cells) to hemoglobin manufacturers and assist in the distribution of the final product. Our survey suggests there will be no consumer price resistance for hemoglobin solutions within the suggested price range of $225–300 per unit. The public would benefit from the quality-enhancing nature of this new product, so the results might be both good economics and good medicine. Currently, hospitals are occasionally forced to cancel surgery because of an insufficient supply of blood, a problem that could get worse in the short run. The future of hemoglobin solutions offers interesting challenges and opportunity for everyone concerned with technology assessment and health policy. The diffusion of this new technology would be an excellent case study for the new federal Agency for Health Care Research and Policy in the United States.

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