

## Where to read more

- For updated information about the advance market commitment, please visit the Center for Global Development Making Markets for Vaccines website at [www.cgdev.org/vaccine](http://www.cgdev.org/vaccine). This website also has links to other resources.
- For an easy-to-use spreadsheet model to calculate estimates of cost-effectiveness and total revenues for malaria, HIV and tuberculosis, please visit [www.cgdev.org/vaccine](http://www.cgdev.org/vaccine).
- For a more detailed explanation of the theory underlying the advance market commitment, see Kremer, M. and R. Glennerster. 2004. *Strong Medicine: Creating Incentives for Pharmaceutical Research on Neglected Diseases*. Princeton, N.J.: Princeton University Press.
- For a more thorough discussion of some of the design issues for an advance market commitment, see Berndt, E. and J. Hurvitz. Forthcoming. "Vaccine Advance Purchase Agreements for Low-income Countries: Practical Issues." *Health Affairs*.
- For a detailed explanation of the estimates of cost-effectiveness and overall costs of an advance market commitment, see Berndt, E., R. Glennerster, M. Kremer, J. Lee, R. Levine, G. Wezsacker and H. Williams. 2005. "Advance Purchase Commitments for a Malaria Vaccine: Estimating Costs and Cost Effectiveness." Center for Global Development, Washington, D.C., available at [www.cgdev.org/vaccine](http://www.cgdev.org/vaccine).

# Notes

## Summary

1. Though most of this report is concerned with vaccines, the discussion in this section also applies to R&D in drugs and diagnostic tools. We use the term “medicines” to mean drugs and vaccines.

2. Global Forum for Health Research (2004a).

3. Known in the jargon as product development public-private partnerships, or PDPPPs.

4. We have coined the term “advance market commitment” to distinguish this proposal from a commitment that guarantees firms sales in advance.

## Chapter 1

1. Against diphtheria-tetanus-pertussis (DTP combinations), measles-mumps-rubella (MMR) and polio.

2. Measles Initiative (2005).

3. *Haemophilus influenzae* type B.

4. About \$3 per dose for products that combine Hib with other antigens.

5. Davey (2002).

6. The Bacille Calmette–Guérin (BCG) vaccine protects against meningitis and disseminated tuberculosis. It has existed for 80 years and is widely used. However, it does not prevent primary infection and, more importantly, does not prevent reactivation of latent primary infection, the main source of bacillary spread in the community. The impact of BCG vaccination on transmission of *Mycobacterium tuberculosis* is therefore limited. The World Health Organization (2004a) says, “the development of efficient, safe and affordable vaccines against TB [tuberculosis] must remain a global priority.”

7. DTwP coverage in OECD countries has fallen from 90% to 34% as they now use DtaP (diphtheria, tetanus and acellular pertussis)—a more costly product that is thought to have a marginally better safety record and a more reliable production profile.

8. CVI Forum (1999), p. 6.

9. DiMasi, Hansen and Grabowski (2003).

10. Mercer Management Consulting (2002).

11. GAVI (2005b).

12. WHO (2003a).

13. Batson (2001).

14. Marketletter (2002).

15. Economists call this a problem of “time inconsistency” because the best policy to pursue changes over time, in a way that can be anticipated at the outset. Predicting a future change in policy, economic actors adjust their behavior today. It is typically solved by some form of institutional pre-commitment that prevents the authorities from “re-optimizing” in the later phase. An advance market commitment would provide such a commitment in this case.

16. Pecoul and others (1999), p. 364. Two of 13 are updated versions of previous products; two are the result of military research; and five come from veterinary research.

## Chapter 2

1. We define “commercial investment” as investment by the for-profit sector, in the expectation of commercial returns.

2. Ernst and Young LLP (2000), p. 47.

3. Widdus and White (2004).

4. Michaud and Murray (1996).

5. Global Forum for Health Research (2004b).

6. Joint Economic Committee (2000).

7. NIH (2001).

8. PhRMA (2005).

9. National Science Foundation (2003).

10. Department of Defense (2004), p. 42.

11. Pecoul and others (1999), p. 364. Two of 13 are updated versions of previous products; 2 are the result of military research; and 5 come from veterinary research.

12. Acemoglu and Linn (2004).

13. See the MVI website [www.malariavaccine.org](http://www.malariavaccine.org) for details.

14. See the IAVI website [www.iavi.org](http://www.iavi.org) for details.
15. See the Aeras website [www.aeras.org/spotlight/gates829.html](http://www.aeras.org/spotlight/gates829.html) for details.
16. Sander and Widdus (2004).
17. DiMasi, Hansen and Grabowski (2003).
18. Malaria Vaccine Initiative (2004).
19. For example, these diseases include Huntington's disease, myoclonus, ALS (Lou Gehrig's disease), Tourette syndrome and muscular dystrophy.
20. Lichtenberg and Waldfoegel (2003).
21. Henkel (1999).
22. Details of the procurement of a meningococcal C vaccine were provided in private communications by Angeline Nanni, formerly with Baxter and now with GAVI's Pneumo ADIP, and with David Salisbury, Principal Medical Officer of U.K.'s Department of Health.
23. Finkelstein (2003, 2004).
24. A caveat is that sales of this intranasal flu vaccine have been lower than expected, likely at least in part due to a high pricing strategy by the manufacturer.
25. Note that this is not guaranteed purchase of any particular product but a guarantee of funds available for qualified products.
26. IFPMA (2004).
5. These estimates are somewhat controversial. See McCarthy, Wolf and Wu (1999) and Gallup and Sachs (2000).
6. Van de Perre and Dedet (2004).
7. The vaccine was originally developed in 1983 by the Walter Reed Army Institute of Research.
8. See the Rotavirus Vaccine Program website [www.rotavirusvaccine.org](http://www.rotavirusvaccine.org).
9. Rotashield, the world's first rotavirus vaccine, was licensed for use in the United States in 1998. Prior to licensing, clinical trials in the United States, Finland and Venezuela had found it to be 80–100% effective at preventing severe rotavirus diarrhea, and researchers had detected no statistically significant serious adverse effects. But Wyeth, the manufacturer of Rotashield, withdrew the vaccine from the market in 1999, after it was discovered that it might have contributed to an increased risk of intussusception, or bowel obstruction, in 1 of every 12,000 vaccinated infants (CNN 2004).
10. See the ADIP website [www.pneumoadip.org](http://www.pneumoadip.org).
11. Apart from the modest cost for the institutional arrangements—that is, the cost of the Independent Adjudication Committee.

### Chapter 3

1. Some pull proposals, such as wildcard patent extensions or full patent buyouts, involve winner-take-all prizes. Academic literature on pull proposals has highlighted the difficulty with this approach. The main arguments are set out in chapter 4.
2. Clinical trials in developing countries are needed to ensure that a vaccine is safe and effective against the strains of the disease prevalent in the region.
3. Acemoglu and Linn (2004).
4. See the MVI website [www.malariavaccine.org](http://www.malariavaccine.org).

### Chapter 4

1. *Force majeure* is a standard contracting clause that declares the contract null and void—and neither party liable for damages—if unforeseeable events fundamentally change the landscape in which the contract was written.

### Chapter 5

1. Acemoglu and Linn (2004).
2. Grabowski, Vernon and DiMasi (2002) note that this is a comprehensive sample of the new chemical entities originating from and developed by the pharmaceutical industry that were introduced into the United States in 1990–94. Due to data limitations, we are unable to address whether the sales revenues of this

sample of self-originated new chemical entities is a representative sample of the sales revenues of all commercial pharmaceutical products. Sales revenue data from a larger sample of products are available from (for example) IMS Health or Scott Levin Associates. Further work could examine this and other potential sources of larger samples of sales revenue data.

3. Berndt and others (2005). Note that Grabowski, Vernon and DiMasi (2002) use this sales revenue data in combination with estimates of the cost of pharmaceutical development in order to estimate total returns; we did not use these cost of development estimates (nor any other cost of development estimates) in our analysis. The \$3.1 billion figure reflects an assumed industry-wide cost of capital (that is, earnings foregone on other investment opportunities) of 8% (close to the annual average return on the stock market) and a downward adjustment of 10% for lower marketing expenditures. Rosenthal and others (2002) estimate that marketing expenditures relative to sales have remained relatively constant at 15%; however, promotion/sales ratios are lower globally, and this 15% figure is also partly the result of an accounting nuance where the values of free samples given to physicians are assessed at average retail price rather than manufacturing price. Hence a 10% reduction for marketing expenditures seems appropriate.

4. Berndt and others (2005). We project a total market of \$750 million in net present value of revenues (2004) dollars in high- and middle-income countries. This estimate is based on annual purchases of malaria prophylaxis drugs, as presumably people would be willing to pay comparable amounts for a malaria vaccine as for malaria prophylaxis drugs. An estimate from the

popular press (Reuters 2003) and correspondence with Pfizer suggest the annual market for malaria prophylaxis drugs from sales to travelers and tourists from developed countries and the military could be as much as \$200 million, but others cite much lower figures. If a vaccine captured \$100 million in peak sales and the profile of sales over time followed that of the average product in the Grabowski, Vernon and DiMasi (2002) sample, the total net present value of those sales would be about \$750.7 million (assuming an 8% cost of capital). Adding in \$100 million of additional revenues from private sales in low- and middle-income countries yields a default of \$850 million in net present value of revenues outside the commitment program.

5. It is a coincidence that the \$15 cost per DALY is the same as the \$15 price per course of treatment.

6. Berndt and others (2005).

## Chapter 6

1. Acemoglu and Linn (2004).

## Chapter 7

1. Financial Reporting Standard 12 Provisions, Contingent Liabilities and Contingent Assets, September 1998.
2. Glennerster and Kremer (2000).
3. IDA terms are a 10-year grace period, a 0% interest rate, and maturities of 35 or 40 years.
4. The exception to this is if no product in a given category has been prequalified.
5. UNICEF (2002).

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## Appendix A

## Abbreviations

<b>ACIP</b>	Advisory Committee on Immunization Practices	<b>IFF</b>	International Financing Facility
<b>ADIP</b>	Accelerated Development and Introduction Plans	<b>IFFIm</b>	International Finance Facility for Immunization
<b>AIDS</b>	acquired immunodeficiency syndrome	<b>IFPMA</b>	International Federation of Pharmaceutical Manufacturers and Associations
<b>BCG</b>	Bacille Calmette–Guérin—a vaccine for tuberculosis	<b>IMCI</b>	Integrated Management of Childhood Illness
<b>BIO</b>	Biotech Industry Organization	<b>IOWH</b>	Institute for OneWorld Health
<b>CDC</b>	Centers for Disease Control and Prevention	<b>IPM</b>	International Partnership for Microbicides
<b>CEA</b>	Council of Economic Advisors	<b>IPR</b>	intellectual property rights
<b>CVI</b>	Children’s Vaccine Initiative	<b>MDP</b>	Microbicide Development Project
<b>DALY</b>	disability-adjusted life year	<b>MMV</b>	Medicines for Malaria Venture
<b>DFID</b>	Department for International Development	<b>MVI</b>	Malaria Vaccine Initiative
<b>DNDi</b>	Drugs for Neglected Diseases Initiative	<b>NIAID</b>	National Institute of Allergy and Infectious Diseases
<b>DTaP</b>	diphtheria, tetanus and acellular pertussis	<b>NIH</b>	National Institutes of Health
<b>DTP</b>	diphtheria, tetanus and pertussis	<b>OPV</b>	oral polio vaccine
<b>DTwP</b>	diphtheria, tetanus and whole-cell pertussis	<b>PDPPPs</b>	product development public-private partnerships
<b>EMVI</b>	European Malaria Vaccine Initiative	<b>PDVI</b>	Pediatric Dengue Vaccine Initiative
<b>EPI</b>	Expanded Programme on Immunization	<b>PhRMA</b>	Pharmaceutical Research and Manufacturers of America
<b>FDA</b>	Food and Drug Administration	<b>R&amp;D</b>	research and development
<b>FRS</b>	Federal Reporting Standard	<b>SAAVI</b>	South African AIDS Vaccine Initiative
<b>GAVI</b>	Global Alliance for Vaccines and Immunization	<b>U.K.</b>	United Kingdom
<b>GDP</b>	gross domestic product	<b>U.S.</b>	United States
<b>GMP</b>	Global Microbicide Project	<b>UN</b>	United Nations
<b>GNP</b>	gross national product	<b>UNICEF</b>	United Nations Children’s Fund
<b>HepB</b>	hepatitis B	<b>USAID</b>	United States Agency for International Development
<b>HHVI</b>	Human Hookworm Vaccine Initiative	<b>VFC</b>	Vaccines for Children
<b>Hib</b>	haemophilus influenzae type B	<b>WHO</b>	World Health Organization
<b>HIV</b>	human immunodeficiency virus		
<b>IAC</b>	Independent Adjudication Committee		
<b>IAVI</b>	International AIDS Vaccine Initiative		
<b>IDA</b>	International Development Association		

## Appendix B

# Objectives of the Working Group

The Advance Market Commitment (originally “Pull Mechanisms”) Working Group is a policy research group convened by the Global Health Policy Research Network at the Center for Global Development to explore the feasibility of advance guarantee agreements as a tool for stimulating research, development and production of vaccines for neglected developing-country diseases. Funding for Working Group meetings, analytic work and consultations was provided under a grant from the Bill & Melinda Gates Foundation.

Because the power and limitations of push mechanisms are reasonably well understood, the Working Group has focused exclusively on whether and how to put into operation advance guarantees as an *additional* new tool for global health products. The results of this work are intended primarily to inform the donor community, which may wish to move toward implementation of such an arrangement as one of several instruments to improve access to affordable vaccines for the developing world.

The Working Group was convened solely for the purpose of exploring the practicality and value of advance contracting; it does not have and will not seek the legal status, the budget or the

mandate to implement such an agreement. Members of the Working Group were selected for their knowledge and expertise, and participate on a voluntary basis in their individual capacities.

We focused exclusively on vaccines in this Working Group for a number of reasons. First, vaccines are among the most cost-effective of health interventions, and immunization programs have been shown to be enormously successful. Second, a key constraint to even greater effectiveness of immunization programs is availability of and access to new products related to the specific needs of children in the developing world. And finally, vaccines are purchased mainly by the public sector and development of new vaccines is a global public good so it is appropriate for donors to be thinking about the most effective ways to channel their immunization funds. We did not choose vaccines because it is the only area where advance contracting would work—many of the principles outlined in this report may be transferable to drugs or diagnostics with some modifications.

Although the Working Group is not expected to continue after the publication of this report, resources related to the group’s work will be available at the Center for Global Development’s website ([www.cgdev.org/vaccine](http://www.cgdev.org/vaccine)).

## Appendix C

# Profiles of Working Group members

### **Abhijit Banerjee**, Massachusetts Institute of Technology

Abhijit Banerjee is the Ford Foundation Professor of Economics in the Department of Economics at Massachusetts Institute of Technology, the Director of the Poverty Action Lab and the ex-President of the Bureau for Research in Economic Analysis and Development. Previously, he taught at Princeton University and Harvard University before joining the Massachusetts Institute of Technology faculty in 1996. He received the Malcolm Adeshesiah Award in 2001 and the Mahalanobis Memorial Medal in 2000. He is a member of the Governing Council of the Econometric Society and the American Academy of Arts and Sciences, and he has been a Guggenheim Fellow and Alfred P. Sloan Research Fellow. His areas of research are development economics, the economics of financial markets and the macroeconomics of developing countries.

### **Amie Batson**, World Bank

Amie Batson is a Senior Health Specialist in the Health, Nutrition and Population unit of the World Bank. She is also the co-chair of the Financing Task Force of the Global Alliance for Vaccine and Immunization charged with supporting governments and international partners to improve sustainable financing, and exploring innovative financing mechanisms to accelerate the development and introduction of priority vaccines in the developing world. Prior to joining the World Bank, she was a joint World Health Organization/United Nations Children's Fund staff member in the Global Programme for Vaccines. She led the work on public-private partnerships for vaccines, launching a new relationship and strategies based on the underlying economics of manufacturing.

### **Ernst Berndt**, Massachusetts Institute of Technology

Ernst Berndt is the Louis B. Seley Professor of Applied Economics at the Massachusetts Institute of Technology's Sloan School of

Management. He also is co-director of the Harvard–Massachusetts Institute of Technology Health Sciences and Technology Biomedical Enterprise Program and directs the National Bureau of Economic Research Program on Technological Progress and Productivity Measurements.

### **Lael Brainard**, Brookings Institution

Lael Brainard is Founding Director of the Poverty and Global Economy Initiative at the Brookings Institution, where she holds the New Century Chair in International Economics. She served as Deputy National Economic Adviser and Chair of the Deputy Secretaries Committee on International Economics during U.S. President Bill Clinton's administration. As the U.S. "Sherpa" to the G-7/G-8, she is credited with shaping the 2000 G-8 Development Summit, which included developing country leaders for the first time and laid the foundations for the Global Fund to Fight AIDS, Tuberculosis and Malaria. Before coming to Washington, she served as Associate Professor of Applied Economics at the Massachusetts Institute of Technology's Sloan School of Management. Previously, she worked at McKinsey and Company advising clients on strategic challenges. She is the recipient of a White House Fellowship and a Council on Foreign Relations International Affairs Fellowship, and a member of the Council on Foreign Relations and the Board of Wesleyan University.

### **David Cutler**, Harvard University

David Cutler is Associate Dean of Social Sciences and Professor of Economics in the Department of Economics and Kennedy School of Government at Harvard University. He served on the Council of Economic Advisers and the National Economic Council during U.S. President Bill Clinton's administration and advised the presidential campaigns of Bill Bradley and John Kerry. Among other affiliations, he has held positions with the National Institutes of Health and the National Academy of Sciences. Currently, he is a Research Associate at the National Bureau of Economic

Research and a member of the Institute of Medicine. He is the author of *Your Money or Your Life: Strong Medicine for America's Health Care System*.

### **David Gold**, Global Health Strategies

David Gold is an attorney and principal of Global Health Strategies. Most recently, he was Vice President for Policy and Public Support at the International AIDS Vaccine Initiative, where he oversaw the creation of its global policy and advocacy programs, as well as its regional programs in North America, Europe, Japan and Latin America. He is also co-founder of the AIDS Vaccine Advocacy Coalition, a consumer-based organization that advocates for AIDS vaccine development and delivery. From 1991–95 he headed the Medical Information Program at Gay Men's Health Crisis, the world's first and largest AIDS organization, and edited its newsletter on HIV therapies, *Treatment Issues*. He has also served on research advisory panels for a number of different organizations including the World Health Organization, the United Nations, the U.S. National Institutes of Health and a number of pharmaceutical companies.

### **Peter Hutt**, Covington & Burling

Peter Barton Hutt is a senior counsel in the Washington, D.C., law firm of Covington & Burling, specializing in food and drug law and teaches Food and Drug Law each winter term at Harvard Law School. He is the co-author of *Food and Drug Law: Cases and Materials*, and was Chief Counsel for the Food and Drug Administration from 1971 to 1975. He is a member of the Institute of Medicine of the National Academy of Sciences, has served on the Institute of Medicine Executive Committee, and other National Academy of Sciences and Institute of Medicine committees. He serves on the Panel on the Administrative Restructuring of the National Institutes of Health. He serves on a wide variety of academic and scientific advisory boards and on the Board of Directors of venture capital startup companies.

### **Randall Kroszner**, University of Chicago

Randall S. Kroszner is Professor of Economics at the Graduate School of Business of the University of Chicago. He is Editor of the *Journal of Law and Economics* and Associate Director of the George J. Stigler Center for the Study of the Economy and the State. He also is a Faculty Research Fellow of the National Bureau of Economic Research and a Visiting Scholar at the American Enterprise Institute. He served as a Senate-confirmed member of the President's Council of Economic Advisers from 2001 to 2003. While on the council, he was involved in policy formulation for a wide range of domestic and international issues, including the Millennium Challenge Account and economic growth and development. He has served as a consultant to the International Monetary Fund, the World Bank, the Inter-American Development Bank, the Swedish Finance Ministry, the Board of Governors of the Federal Reserve System and several Federal Reserve Banks, and currently serves as a Research Consultant for the Federal Reserve Bank of Chicago. He has been a visiting professor at the Stockholm School of Economics, the Free University of Berlin and the Institute for International Economic Studies at the University of Stockholm. His research interests include corporate governance, conflicts of interest in financial services firms, banking and financial regulation, debt restructuring and forgiveness, international financial crises and political economy.

### **Thomas McGuire**, Harvard University

Thomas McGuire is Professor of Health Economics in the Department of Health Care Policy at Harvard Medical School. His research focuses on the design and impact of health care payment systems, the economics of health care disparities and the economics of mental health policy. He has contributed to the theory of physician, hospital and health plan payment. His current research includes application of theoretical and empirical methods from labor economics to the area of health care disparities. For more than 25 years, he has conducted academic and policy research on

the economics of mental health. He is a member of the Institute of Medicine, and a co-editor of the *Journal of Health Economics*.

### **Tomas Philipson, U.S. Food and Drug Administration**

Tomas Philipson is a professor in the Harris School of Public Policy at the University of Chicago and a faculty member in the Department of Economics and the Law School. His research focuses on health economics. During 2003/04, he served as the Senior Economic Advisor to the Commissioner of the Food and Drug Administration and currently serves as the Senior Economic Advisor to the Administrator of the Centers for Medicare and Medicaid Services. Previously, he was a visiting faculty member at Yale University and a visiting fellow at the World Bank in the winter of 2003. He is a co-editor of the journal *RAND Forums in Health Economics* of Berkeley Electronic Press and is affiliated with a number of professional organizations, including the National Bureau of Economic Research, the George J. Stigler Center for the Study of the Economy and the State, the Robert Wood Johnson Clinical Scholars Program, the Northwestern/University of Chicago Joint Center for Poverty Research, the National Opinion Research Center and the American Economic Association.

### **Leighton Read, Alloy Ventures**

Leighton Read is a General Partner at Alloy Ventures, following 14 years as a biotechnology entrepreneur and investor. He co-founded Affymax NV and founded Aviron, a biopharmaceutical company focused on vaccines for infectious disease, where he served as Chairman and CEO until 1999 and Director until its acquisition by MedImmune in 2002. He was also a partner in Interhealth Limited, an investment partnership. He is a director of Avidia, Alexza and Cambrios Technologies and has served as director for a number of other biotechnology companies and on the executive committee of the Biotechnology Industry Organization. He has

also won several awards as co-inventor of technology underlying the Affymetrix GeneChip™.

### **Tom Scholar, International Monetary Fund**

Tom Scholar is the United Kingdom Executive Director to the International Monetary Fund and the World Bank. He also serves as Minister (Economic) at the British Embassy, Washington. Previously, he was Economic Adviser to the H.M. Treasury and Principal Private Secretary to the Chancellor of the Exchequer at the H.M. Treasury.

### **Rajiv Shah, Bill & Melinda Gates Foundation**

Rajiv Shah is the deputy director for Strategic Opportunities and Evaluation at the Bill & Melinda Gates Foundation. Previously, he managed the global health program's policy and finance portfolio, helped manage the program's largest grant effort, the Vaccine Fund, and shaped overall strategy for engaging with bilateral and multilateral financial institutions. He served as the health care policy advisor on the Gore 2000 presidential campaign in Nashville, Tennessee, and on Philadelphia Mayor John Street's New Century Committee. He started, managed and sold a health care consulting firm, Health Systems Analytics, which served clients including some of the largest health systems in the country. In 1995 he co-founded Project IMPACT, an award-winning national nonprofit that conducts leadership, mentoring, media and political activism activities.

### **David Stephens, Emory University**

David Stephens is Professor of Medicine, Microbiology and Immunology and Epidemiology; Director, Division of Infectious Diseases, Department of Medicine; and Executive Vice Chair of the Department of Medicine, Emory University School of Medicine, and holds the Stephen W. Schwarzman Distinguished Professorship in Internal Medicine at Emory University. He has contributed to the development of meningococcal, pneumococcal and *Bacillus*

*anthracis* vaccines including efforts to develop a meningococcal conjugate vaccine that is affordable for countries in Sub-Saharan Africa. He has also helped lead efforts to address vaccines for biodefense and emerging infections serving as the Executive Director of the Centers for Disease Control and Prevention–sponsored Southeastern Center for Emerging Biological Threats, as the Emory Principal Investigator for the National Institutes of Health–sponsored Southeastern Research Center of Excellence in Biodefense and Emerging Infections and as director of a National Institutes of Health–sponsored new pathway center at Emory for interdisciplinary research in vaccinology. He is a past chair of the Food and Drug Administration’s National Vaccine Advisory Committee and has more than 200 publications in infectious diseases, molecular pathogenesis, vaccines and epidemiology.

### **Wendy Taylor**, BIO Ventures for Global Health

Wendy Taylor is the Executive Director of BIO Ventures for Global Health. Previously, she was the Director of Regulatory Affairs and Bioethics for the Biotechnology Industry Organization (BIO) where she spearheaded BIO’s global health initiative. Joining BIO in November 2001, she negotiated on behalf of the biotech industry the third reauthorization of the Prescription Drug User Fee Act with the Food and Drug Administration; established and led BIO’s Regulatory Affairs Committee and worked with the Food and Drug Administration to address a range of regulatory issues important to the biotech industry. She also has extensive experience in the executive and legislative branches of the U.S. government, including positions at the Office of Management and Budget, the U.S. Department of Health and Human Services and the U.S. House Committee on Ways and Means.

### **Adrian Towse**, Office of Health Economics

Adrian Towse is the Director of the Office of Health Economics. He is a Visiting Professor at the University of York and a

Non-executive Director of the Oxford Radcliffe Hospitals NHS Trust, one of the United Kingdom’s largest hospitals. His current research interests include the use of “risk-sharing” arrangements between health care payers and pharmaceutical companies; the economics of pharmacogenetics; economic issues around access to, and R&D for the development of, treatments for less developed country diseases; the economics of medical negligence; and measuring productivity in health care.

### **Sean Tunis**, U.S. Department of Health and Human Services

Sean Tunis is currently the Director of the Office of Clinical Standards and Quality and Chief Medical Officer at the Centers for Medicare and Medicaid Services. He oversees several major elements of the Centers for Medicare and Medicaid Services quality and clinical policy portfolio, including the development of national coverage policies and quality standards for Medicare and Medicaid providers, and serves as a senior advisor to the administrator on clinical and scientific policy. Previously, he was a senior research scientist with the Lewin Group, Director of the Health Program at the Congressional Office of Technology Assessment and a health policy advisor to the U.S. Senate Committee on Labor and Human Resources. He holds an adjunct faculty position in the Department of Medicine at the Johns Hopkins School of Medicine, and continues to practice as a part-time emergency room physician in Baltimore, Md.

### **Sharon White**, U.K. Department for International Development

Sharon White is presently Director of Policy at the U.K. Department for International Development. Previously she held a series of other posts in the United Kingdom and international public sector including senior economist in the Poverty Reduction Group of the World Bank, adviser to Prime Minister Tony Blair on

U.K. welfare reform and First Secretary (Economic) at the U.K. Embassy to the United States.

### **Victor Zonana**, Global Health Strategies

Victor Zonana is principal and co-founder of Global Health Strategies. Previously, he was founding Vice President for Communications of the Vaccine Fund and Vice President for Communications of the International AIDS Vaccine Initiative between 1998 and 2001. During the first five years of U.S. President Bill Clinton's administration, he served as Deputy Assistant Secretary for Public Affairs of the Department for Health and Human Services. Before joining the government, he was a journalist for *The Wall Street Journal* and *The Los Angeles Times*. He was the 1990 winner of the John Hancock award for distinguished financial journalism and was nominated twice for a Pulitzer Prize.

### **Staff**

#### **Owen Barder**, Center for Global Development

Owen Barder is a Senior Program Associate at the Center for Global Development. He has previously worked in the U.K. Treasury, No. 10 Downing Street, the U.K. Department for International Development and the South African Treasury.

#### **Gargee Ghosh**, Bill & Melinda Gates Foundation

Gargee Ghosh is a Program Officer and Economist with the Bill & Melinda Gates Foundation, where she works primarily on innovative financing and delivery for vaccines and immunization. She helps manage the foundation's work with the Global Alliance for Vaccines and Immunization, and particularly its funding arm the Vaccine Fund. Prior to joining the foundation, she worked with the Center for Global Development's Global

Health Policy Research Network as the project manager for its Pull Mechanisms Working Group. She also spent several years as a management consultant with McKinsey and Company in New York and London working with the firm's health care and nonprofit clients around the world.

### **Co-chairs**

#### **Alice Albright**, Vaccine Fund

Alice Albright is Vice President and Chief Financial Officer of the Vaccine Fund. Previously, she worked in international financial markets with an emphasis on emerging markets. From 1999 to 2001, she was a Principal in the Leveraged Buy-Out practice of the Carlyle Group in Washington, D.C. She was a Vice President at JP Morgan from 1989 to 1999 where she held various positions in the emerging markets, corporate finance, credit portfolio management and lending areas. From 1987 to 1989, she was an Associate in Bankers Trust's Latin American Merchant Bank. From 1985 to 1987, she worked as a management consultant at Citicorp, conducting financial management assignments in Latin America and Europe. She is a Chartered Financial Analyst.

#### **Michael Kremer**, Harvard University

Michael Kremer is the Gates Professor of Developing Societies in the Department of Economics at Harvard University and Senior Fellow at the Brookings Institution. He is a Fellow of the American Academy of Arts and Sciences and a recipient of a MacArthur Fellowship and a Presidential Faculty Fellowship. His recent research examines education and health in developing countries, immigration and globalization. He and Rachel Glennerster recently published *Strong Medicine: Creating Incentives for Pharmaceutical Research on Neglected Diseases*. His articles have been published in journals including the *American Economic Review*, *Econometrica* and the *Quarterly Journal of Economics*. He



previously served as a teacher in Kenya. He founded and was the first executive director of WorldTeach, a nonprofit organization that places more than 200 volunteer teachers annually in developing countries (1986–89).

### **Ruth Levine, Center for Global Development**

Ruth Levine, Senior Fellow and Director of Programs at the Center for Global Development, is a health economist with 14 years' experience in health and family planning financing issues in Latin America, eastern Africa, the Middle East and South Asia. She currently leads the Center's Global Health Policy Research Network and is principal staff on the Millennium Project Educa-

tion and Gender Equality Task Force. Before joining the Center for Global Development, she designed, supervised and evaluated health-sector loans at the World Bank and the Inter-American Development Bank. She also conducted research on the health sector and led the World Bank's knowledge management activities in the area of health economics and finance between 1999 and 2002. Since 2000, she has worked with the Financing Task Force of the Global Alliance on Vaccines and Immunization. Between 1997 and 1999, she served as the adviser on the social sectors in the Office of the Executive Vice President of the Inter-American Development Bank. She is co-author of *The Health of Women in Latin America and the Caribbean* and *Millions Saved: Proven Successes in Global Health*.

## Appendix D

# Individuals consulted

During the course of this project, many individuals offered comments, critiques and suggestions. These individuals are listed below, but bear no responsibility for the content or recommendations of this report. We apologize for any omissions.

- Pedro Alonso, Scientific Director, Manhica Health Centre, Manhica, Mozambique and Head, Center for International Health, University of Barcelona, Spain
- Bill Antholis, German Marshall Fund U.S.
- John Audley, German Marshall Fund U.S.
- Ripley Ballou, Clinical R&D, GlaxoSmithKline Biologicals, Rixensart, Belgium
- Luis Barreto, Aventis-Pasteur
- Carolyn Bartholomew, then Chief of Staff for Congresswoman Nancy Pelosi
- Simon Best, Ardana
- Alan Brooks, Program for Accessible Technologies in Health
- Graham Brown, Department of Medicine, University of Melbourne, Australia
- Josh Buger, Vertex
- Chip Cale, GSK Biologicals
- Sandra Chang, Tropical Medicine and Medical Microbiology, University of Hawaii
- Rob Chess, Nectar Therapeutics
- Chris Collins, Joint United Nations Programme on HIV/AIDS
- Tim Cooke, Mojave Therapeutics
- Martinho Dgedge, Expanded Program on Immunization Manager, Mozambique
- Carter Diggs, Senior Technical Advisor, U.S. Agency for International Development
- Steve Drew, GSK Biologicals
- Laura Efras, Merck Vaccine Division
- Thomas Egwang, MedBiotech Laboratories, Uganda
- Ibrahim El Hassan, Institute of Endemic Diseases, University of Khartoum, Sudan
- Howard Engers, Armauer Hansen Research Institute, Ethiopia
- Elaine Esber, Merck Vaccine Division
- Sarah Ewart, Malaria Vaccine Initiative
- Andrew Farlow, University of Oxford
- David Fleming, then Centers for Disease Control and Prevention; now Bill & Melinda Gates Foundation
- Michael Fleming, Merck Vaccine Division
- Martin Friede, Initiative for Vaccine Research, World Health Organization
- Joel Friedman, Center for Budget Policy and Priorities
- Geno Germano, Wyeth
- Roger Glass, Centers for Disease Control and Prevention
- Michel Greco, formerly Aventis
- Shanelle Hall, United Nations Children's Fund, Supply Division
- Jane Haycock, U.K. Department for International Development
- Rob Hecht, then World Bank, now International AIDS Vaccine Initiative
- Russell Howard, Maxygen
- Suresh Jadhav, Serum Institute
- Stephen Jarrett, United Nations Children's Fund, Supply Division
- Soren Jepsen, European Malaria Vaccine Initiative, Copenhagen, Denmark
- Miloud Kaddar, World Health Organization
- Cheikh Kane, J P Morgan
- Hannah Kettler, Bill & Melinda Gates Foundation
- Marie-Paule Kieny, Director, Initiative for Vaccine Research, World Health Organization
- Wenceslaus Kilama, African Malaria Vaccine Testing Network, Tanzania

- Fred Kironde, Makerere University, Kampala, Uganda
- Andrew Kitua, Director General, National Institute for Medical Research, Tanzania
- Richard Kogan, Center for Budget Policy and Priorities
- Antoniana Krettli, Fiocruz, Brazil
- James Kublin, Merck Vaccine Division
- Steve Landry, Bill & Melinda Gates Foundation
- Odile Leroy, Clinical and Regulatory Affairs, European Malaria Vaccine Initiative
- Orin Levine, Pneumococcal Accelerated Development and Introduction Plan
- Clem Lewin, Chiron
- Adel Mahmoud, Merck Vaccine Division
- Frank Malinoski, Wyeth
- Kevin Marsh, Kenya Medical Research Institute, Kilifi, Kenya
- Sean McElligot, Merck Vaccine Division
- Eunice Miranda, GSK Biologicals
- Marge Mitchell, Merck Vaccine Division
- Melinda Moree, Malaria Vaccine Initiative
- Debbie Myers, GSK Biologicals
- Angeline Nanni, Pneumococcal ADIP
- Thomas Netzer, Merck Vaccine Division
- Tim Obara, Merck Vaccine Division
- Paul Offit, Childrens' Hospital of Philadelphia
- Stewart Parker, Targeted Genetics
- Jerry Parrot, Human Genome Sciences
- Alix Peterson Zwane, University of California, Berkeley
- Gina Rabinovich, Bill & Melinda Gates Foundation
- Patricia Roberts, Malaria Vaccine Initiative
- Una Ryan, Avant Therapeutics Inc
- Jerry Sadoff, Aeras Global TB Vaccine Foundation
- Mark Sanyour, Merck Vaccine Division
- Andrew Segal, Genitrix
- Alan Shaw, Merck Vaccine Division
- Tim Sullivan, Princeton University Press
- Larry Summers, Harvard University
- Jim Tartaglia, Aventis-Pasteur
- Jean Tirole, Institut d'Economie Industrielle
- Thomas Vernon, Merck Vaccine Division
- John Wecker, Rotavirus ADIP
- Lowell Weiss, Bill & Melinda Gates Foundation
- Roy Widdus, Institute for Public Private Partnerships in Health
- Michel Zaffran, World Health Organization

## Appendix E

# A tool to estimate cost effectiveness of an advance market commitment

Michael Kremer and Rachel Glennerster, authors of the recent book *Strong Medicine: Creating Incentives for Pharmaceutical Research on Neglected Diseases*, set out the theoretical underpinnings of pull incentives in more detail. Ernst Berndt and others have developed a spreadsheet model (available for download from the Center for Global Development website at [www.cgdev.org/vaccine](http://www.cgdev.org/vaccine)) that allows users to manipulate all relevant variables in a flexible and user-friendly way, thereby permitting the analysis of a large number of different scenarios.

The spreadsheet allows for the analysis of costs and benefits of commitments for malaria, HIV and tuberculosis vaccines under various assumptions of vaccine characteristics as well as various contract parameters on the price and quantity of vaccines that would be purchased at the initial, high price. The spreadsheet combines these user-entered assumptions with a collection of demographic and disease burden data to estimate the cost per

DALY saved as well as to calculate the net present value of the revenues that would accrue to a vaccine developer.

For example, the user may vary general parameters (such as the discount rate and the cost effectiveness threshold for a DALY), and parameters that define vaccine efficacy and the number of required doses. The user may change the set of countries covered by the program manually, by disease burden and/or using a GNP per capita cutoff. The user can also vary the conditions of adoption, including steady-state adoption rates and the length of time to reach the steady state. A technical guide posted online with the spreadsheet explains the calculations in detail in the order that the worksheets appear in the Microsoft Excel file. Since parameters can be modified and results displayed in the graphical user interface, the user will rarely, if ever, need to refer to these detailed sheets. Berndt and others (2005) discuss both the general results of the spreadsheet analysis and sensitivity checks.

## Appendix F

# Model term sheet for Framework Agreement

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- 1. Parties:** One or more nongovernmental, grant-making organizations (such as a foundation) or governmental grant-making organizations (such as the U.S. Agency for International Development or the U.K. Department for International Development) (each, a **“Funder”**)<sup>1</sup> and one or more pharmaceutical or biotech companies<sup>2</sup> that will work within the Framework (as defined below) to develop eligible vaccine(s) (each, a **“Developer”**).
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- 2. Purpose:** Create a legally binding series of agreements<sup>3</sup> that guarantees the developer(s) of a [\_\_\_\_\_] vaccine<sup>4</sup> that meets the requirements set forth in the agreements a specific price for each qualified sale of the vaccine in certain designated developing countries (the **“Framework”**). The Framework Agreement will clearly state the goals and objectives of the Framework with regard to the target disease, the eligible countries and the affected populations.<sup>5</sup>
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- 3. Benefits to Funder:** Fulfills the Funder’s philanthropic mission (or a statutory or regulatory mandate, in the event Funder is a governmental organization) by giving Developers an economic incentive to (a) select and implement R&D projects that are likely to lead to vaccines developed specifically for diseases concentrated in developing countries, and (b) establish manufacturing capacity for production of such vaccines.
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- 4. Benefits to Developers:** Establishes a specific price for all eligible sales of the vaccine in developing countries that allows the Designated Supplier (as defined below) to cover, over the term of the agreements, R&D costs as well as manufacturing costs and to make an acceptable return on its investment. The guaranteed price will be based on a per-patient dosing regimen to provide the required prophylactic benefit and will be paid on all eligible sales up to the maximum number specified in the Guarantee and Supply Agreement (the **“Maximum Guaranteed Amount”**). For example, if a course of 3 immunizations are required to provide the necessary immunity, the guaranteed price is \$15 and the Maximum Guaranteed Amount is 200 million, then the Developer would receive the guaranteed price of \$15 only upon an eligible sale of all three doses comprising the course of treatment. If the Developer’s total eligible sales equal the Maximum Guaranteed Amount, 600 million doses, or 200 million courses of treatment, then the Developer would receive a total payment of \$3 billion.<sup>6</sup>
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# Notes

1. The Framework Agreement and Guarantee Agreement term sheets were designed to accommodate a variety of Funders, despite the fact that there are substantial differences between governmental and nongovernmental organizations in areas such as funding capacity and ability to contractually commit to the Guarantee Agreement. We concluded that traditional commercial mechanisms for ensuring compliance, such as letters of credit or escrow arrangements, would be unattractive to potential Funders as they would result in increased transaction costs and unnecessarily tie up funds that could be made available for more immediate opportunities. Instead, we designed a bilateral contract structure, which would permit the Developer to pursue standard contract remedies, such as money damages and specific performance, if the Funders fail to satisfy their financial commitments.
2. The Framework and Guarantee term sheets were designed to allow participation by both pharmaceutical companies and biotechnology companies. We considered, but did not incorporate, an alternative funding system recommended by a few of the biotechnology companies interviewed that would provide for interim payments, upon the achievement of certain predetermined milestones, to create incentives for research and early-stage development activities and encourage venture capital investment in emerging companies committed to the Framework. We intend that intermediate incentives of this kind will be created by the commercial activities of Developers in the expectation of being remunerated through sales of vaccines under the Guarantee Agreement.
3. Initially, the Working Group considered establishing the Framework Agreement as a form of unilateral agreement. A unilateral agreement is an offer by one party, in this case the Funder, which only becomes a contract when it is accepted by the other party, the offeree or in this case the Developer. A unilateral agreement permits the offeror to withdraw its offer prior to acceptance, and what constitutes acceptance is not always clear, particularly in this context. We thought this risk might create too much uncertainty for the Developer and thereby dilute the effect of the commitment. The Framework Agreement as reflected in this term sheet would be bilateral agreement, which would be binding on the Funders as soon as one or more Developers sign on.
4. The Working Group initially intended that the Framework Agreement and Guarantee Agreement term sheets would be used for both late-stage and early-stage vaccine candidates. However, on further consideration, we decided that a form approach did not make sense for late-stage vaccine candidates, given the fact that specific Developers and Approved Vaccines had been identified for Rotavirus, and the recognition that each Developer had specific needs and objectives. Instead, the Working Group recommended that the Developers and the Funders directly negotiate long-term supply or other appropriate arrangements to ensure reliable, affordable supply to meet the long-term needs of Eligible Countries, while providing appropriate rewards for the vaccine developer.
5. Each Framework Agreement will establish a specific price for qualified sales of an Approved Vaccine, by supplementing the “base price” paid by a vaccine purchaser (such as UNICEF on behalf of the developing country) up to a certain fixed amount.
6. We concluded that the price guarantee should be for “per course of treatment” rather than “per dose.” This approach provides incentives to ensure that all doses of multiple dose vaccines are administered, and encourages the development of vaccines requiring fewer doses where scientifically possible.

<b>5. Principal Responsibilities of the Funder:</b>	The Funder shall (a) upon satisfaction of the conditions precedent set forth in Section 7, enter into a Guarantee and Supply Agreement (in the form attached to the Framework Agreement) with one or more Designated Supplier(s) (as defined below), <sup>7</sup> (b) fund the operation of the Independent Adjudication Committee (as defined below) in accordance with budgeted amounts, (c) indemnify the members of the Committee for claims and losses arising out of the performance of their duties under the Framework Agreement and the Guarantee and Supply Agreement, <sup>8</sup> (d) retain the Contract Administrators (as defined below) to administer the Framework in accordance with budgeted amounts, (e) maintain in strict confidence any confidential business information submitted to it by the Developers, and (f) agree to be bound by decisions of the Committee acting within the scope of its authority.
<b>6. Principal Responsibilities of Developers:</b>	Each Developer shall (a) provide confidential reports to the Independent Adjudication Committee on the progress of its development efforts at the times specified by the Committee (it is contemplated that these reports would be high-level annual status reports at the outset and would increase in frequency and detail as the development efforts advance), <sup>9</sup> (b) provide such technical information as may be reasonably requested by the Committee in order to confirm that the conditions precedent set forth in Section 7 have been satisfied, and (c) agree to be bound by decisions of the Committee acting within the scope of its authority.
<b>7. Conditions Precedent to Obligations of Funder:</b>	It shall be a condition precedent to Funder's obligation to enter into and perform its obligations under the Guarantee and Supply Agreement that the vaccine meet (a) the technical specifications outlined in Section 8 below, and (b) the usability requirements outlined in Section 9 below. <sup>10</sup>
<b>8. Technical Specifications:</b>	For a vaccine to meet the technical specifications it must, subject to Section 10, satisfy the approval, safety and efficacy requirements set forth in Schedule A.
<b>9. Usability Requirements:</b>	For a vaccine to meet the usability requirements it must, subject to Section 10, satisfy the dosage, means of delivery, storage, shelf life and other requirements set forth in Schedule A.
<b>10. Waiver of Conditions Precedent:</b>	After the effective date of the Framework Agreement the Independent Adjudication Committee may (by a 2/3 vote of its members or at the direction of the Funder) waive or modify the technical specifications or usability requirements in a way that does not materially increase the cost of performance for a Developer. For purposes of illustrating the foregoing, if a specification called for 60% effectiveness, the Committee could, by a 2/3 vote of its members, reduce the requirement to 50% effectiveness, but could not increase it to 70% effectiveness under this provision. <sup>11</sup>

7. Until a vaccine is approved under the conditions set forth in Section 7 of the Framework Agreement term sheet, the Funder is only required to commit to the Framework Agreement, and fund the functions of the Independent Adjudication Committee. Once an Approved Vaccine is identified, the Developer has the right, and the Funder the obligation, to enter into the Guarantee Agreement with respect to that product.
8. Indemnification was deemed to be particularly important to attract qualified members to serve on the Independent Adjudication Committee. It is contemplated that this indemnification would be similar to that which is provided to officers and directors of corporations. Accordingly, the indemnification of the members of the Independent Adjudication Committee may exclude intentional misconduct or actions that are conducted in bad faith or for personal gain.
9. Developers may provide confidential information to the Independent Adjudication Committee in two circumstances. First, Developers would submit progress reports to the Independent Adjudication Committee during the term of the Framework Agreement. These reports will provide a way to evaluate the effectiveness of the mechanism during the research and early development periods. These reports, if not promising, may permit the Funder to withdraw from the Framework Agreement under Section 25 of the term sheet.

Second, for those Developers seeking to participate at a later date, the Framework Agreement requires some evidence that the Developer has a technology or expertise with scientific promise for the development of an Approved Vaccine.
10. Although the Framework Agreement is designed to create an enforceable bilateral contract between the Developers and the Funders, the Funders would not be obligated to enter into the Guarantee Agreement until a product is tendered that meets certain minimum technical specifications, such as approval of both the product and its manufacturing process by a qualified regulatory body and certain safety, efficacy and use requirements.
11. Because there was concern that the Developer should be assured that the Funder could not change the rules of the game after the Framework Agreement was entered into, technical requirements cannot be changed to increase the burden of those requirements, unless there is a significant change in circumstances with respect to the disease that would significantly reduce the need for a vaccine or undermine the specifications, such as a dramatic decrease in disease prevalence, a significant change in disease transmission or progression or a major advancement in treatment. As noted below, these types of changes would be subject to judicial review. Technical requirements may be decreased, however, at the discretion of the Independent Adjudication Committee.



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- 11. Testing and Acceptance:** The Developer shall submit the vaccine to the Independent Adjudication Committee for testing and acceptance. The Committee shall be responsible for making determinations with respect to whether a vaccine tendered by a Developer satisfies the conditions precedent set forth in Section 7, provided that the Independent Adjudication Committee shall have the right to delegate this responsibility to one or more third parties that it determines are qualified to make such determinations and are independent and unbiased, such as, for example, the World Health Organization’s prequalification process.<sup>12</sup> Further, the Committee shall have the right to retain one or more consultants or rely on the actions of governmental or other third parties, such as the United States Food and Drug Administration, in making its determinations. In addition, the Committee shall have authority to grant waivers of, or make modifications to, the application of specific technical specifications or usability requirements as provided in Sections 10 and 22.
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- 12. Designated Supplier:** If the Independent Adjudication Committee determines that the conditions precedent have been satisfied (or if the conditions that have not been satisfied are waived or modified), then (a) the vaccine submitted by the Developer to the Committee shall be deemed an **“Approved Vaccine,”** (b) the Developer of the Approved Vaccine shall be deemed a **“Designated Supplier,”** and (c) if requested by the Designated Supplier, the Funder shall enter into the Guarantee and Supply Agreement with the Designated Supplier within thirty (30) days of the date of the final, written determination of the Committee.<sup>13</sup>
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- 13. Composition of Independent Adjudication Committee:** The Funder shall establish a committee (the **“Independent Adjudication Committee”** or the **“Committee”**), which shall comprise not less than [5] members. Members of the Committee will have expertise in the following fields: (a) immunization practices, (b) public health, (c) vaccinology and vaccine development, manufacturing and commercialization, (d) pediatric and internal medicine, (e) social and community attitudes on immunization, (f) economics, (g) contract law and (h) the vaccine industry, in each case, as applicable, with developing country perspectives. Members of the Committee shall serve a term of [ ] years. Vacancies on the Committee will be filled by the remaining members of the Committee.
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- 14. Actions of the Committee:** Each member of the Independent Adjudication Committee shall have one vote. Fifty percent of the members of the Committee, rounded up, shall constitute a quorum. Except as provided in Sections 10, 20 and 22, all decisions of the Committee shall be made by majority vote of the members at a meeting at which a quorum exists.
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12. The Working Group recognized that it would be extremely costly to create an Independent Adjudication Committee that was fully capable of independently evaluating, approving and monitoring the Approved Vaccines and their ongoing production. Accordingly, the Framework Agreement permits the Independent Adjudication Committee to rely on third parties and their procedures, such as the WHO and its prequalification process.
  
13. As noted above, the Framework Agreement is designed to be self-executing with respect to the Funders, providing the Developers with the right to enter into the Guarantee Agreement on the terms specified in the Framework Agreement. The Framework Agreement is also designed to permit more than one Developer to receive funds under the Guarantee Agreement. For the reasons discussed in the Guarantee Agreement, and more fully in the report, the Working Group determined not to pursue a winner-takes-all approach.

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- 15. Duties of the Committee:** The Committee will (a) seek to identify independent, unbiased and expert-qualified institutions and procedures to assist with determining whether a product meets the technical specifications and usability requirements and that can provide ongoing review of product safety and efficacy and manufacturing, (b) if necessary, designate Approved Regulatory Countries and Approved Manufacturing Countries from time to time, (c) evaluate products presented by Developers to determine if they satisfy the conditions precedent, (d) at its discretion or at the direction of Funder, waive or modify the application of specific technical specifications or usability requirements pursuant to Section 10, (e) if requested or as necessary, conduct multiple bilateral or multilateral meetings with Developer(s) in order to provide information about testing and acceptance procedures, waivers and modifications to the conditions precedent, market demand and supply forecasting, disease epidemiology and other relevant information,<sup>14</sup> (f) using the standards specified in Schedule B, determine whether subsequent vaccines are superior to the original Approved Vaccine, whether for certain target populations, epidemiological conditions or otherwise, and designate new Approved Vaccine(s) and new Designated Supplier(s), (g) after an Approved Vaccine has been designated, monitor the sales and use of such Approved Vaccine for ongoing compliance with the technical specifications and usability requirements set forth in Sections 8 and 9 and decertify any vaccine that is not in material compliance with such specifications and requirements, and (h) determine whether the technical specifications and usability requirements set forth in Sections 8 and 9 or the Maximum Guaranteed Amount or Funder's other payment obligations under the Guarantee and Supply Agreement should be modified in whole or in part based on *force majeure* criteria pursuant to Section 22.
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- 16. Duties of Committee Members:** Each member of the Independent Adjudication Committee shall, in the exercise of its authority under the Framework Agreement, have the same fiduciary duties (including duty of care and duty of loyalty) as the director of a Delaware corporation.<sup>15</sup>
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- 17. Contract Administrator:** The Funder shall retain one or more individuals (each, a “**Contract Administrator**”) to implement the decisions of the Independent Adjudication Committee and to perform such other administrative, support and other tasks as may be assigned by the Committee, subject to the approved budget for administrative expenses.
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- 18. Budget:** The parties shall agree on a budgeting process to ensure that the reasonable expenses of the Independent Adjudication Committee and the Contract Administrators will be reimbursed by Funder.<sup>16</sup>
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14. It is contemplated that the Developers would have the right to consult with the Independent Adjudication Committee, much the same way that companies consult with the FDA in the United States, to discuss the design of clinical trials, the structure of drug approval applications, the country or countries in which such approval will be sought, the possibility of granting waivers and other issues relating to the approval of an Approved Vaccine.
15. The duties of a corporate director under Delaware Law are the duty of loyalty, the duty of care and the duty of good faith. The duty of loyalty requires the director to place the corporation's interests above his or her own. The duty of care requires the director to act with certain minimum level of skill and deliberation. The duty of good faith requires that a director not act with bad faith, or engage in intentional misconduct.
16. A Funder's obligation to reimburse the Independent Adjudication Committee is subject to the requirement that its expenses be reasonable. A Funder may want to give further consideration to mechanisms that would permit it to regulate the cost of the Independent Adjudication Committee without compromising the Independent Adjudication Committee's independence.

<b>19. Addition of New Developers to the Framework:</b>	During the period beginning on the effective date of the Framework Agreement and ending [36] months thereafter, one or more entities may become parties to the Framework Agreement ( <i>i.e.</i> , Developers) upon written acceptance of the terms of the Framework Agreement by such entity. Thereafter, additional entities may become parties to the Framework Agreement upon (a) written approval by the Committee if the new entity has technology or expertise that shows promise for the development of an Approved Vaccine, and (b) written acceptance of the terms of the Framework Agreement by the new entity; provided that no entity may become a party to the Framework Agreement with respect to a product after it commenced clinical trials for such product without the consent of the Funder. <sup>17</sup>
<b>20. Addition of New Designated Suppliers:</b>	The Independent Adjudication Committee may (by a 2/3 vote of its members and using the standards specified in Schedule B) determine that a newly developed vaccine satisfies the conditions precedent in Section 7, subject to its waiver and modification authority, and is superior to the previously selected Approved Vaccine, whether for certain target populations or epidemiological conditions or otherwise. Upon such a determination by the Committee, the Developer of the newly developed vaccine shall have the right to become a party to the Guarantee and Supply Agreement, whereupon the Developer of the new vaccine shall be deemed a “Designated Supplier” and the new vaccine shall be deemed an “Approved Vaccine.” The addition of new Designated Suppliers and Approved Vaccines shall, in each case, be subject to the original Maximum Guaranteed Amount set forth in the Guarantee and Supply Agreement. <sup>18</sup>
<b>21. Reserved Rights of Developer:</b>	Developer reserves all rights, and the Framework shall not apply, to sales of any Approved Vaccine (a) outside the eligible countries identified in the Guarantee and Supply Agreement, and (b) in the military or travelers markets.
<b>22. Force Majeure</b>	In the event that there is a substantial change in circumstances with respect to [disease] in the countries identified in the Guarantee and Supply Agreement, including, without limitation, its incidence, its characteristics or methods for its treatment or prevention, such that the technical specifications outlined in Section 8, or the usability requirements outlined in Section 9 no longer achieve the original objectives, the Committee shall have the right (by a 3/4 vote of its members), using the criteria set forth in Schedule C, to (a) modify the technical specifications or the usability requirements, as applicable, (b) reduce the Maximum Guaranteed Amount or the Funder’s other financial obligations to reflect changes in the number of eligible countries or the incidence of untreated [disease] in those countries, or (c) terminate the Framework Agreement. Unlike other decisions of the Committee, these decisions shall be subject to judicial review by an appropriate forum to determine whether the Committee abused its discretion. <sup>19</sup>
<b>23. Representation and Warranties:</b>	[TBD]

17. These procedures were intended to strike a balance between, on the one hand, permitting companies with promising technology or relevant expertise to participate in the Framework and, on the other hand, discouraging free riders who would operate outside the Framework and sign on only at the last minute. If companies do not sign on to the Framework, the agreement would lose its binding effect. Moreover, it would be difficult for the Funders to monitor the success of the Framework, particularly with respect to research and early development, without the periodic reporting by the Developer required under the Framework Agreement. Funders may wish to strike a different balance, such as allowing companies to join the Framework up until they commence pivotal trials.
18. The Working Group devoted considerable discussion to the question of whether more than one Developer would be permitted to receive payments under the Guarantee Agreement. On the one hand, the Working Group felt that it was important to preserve incentives for product improvements and that it would be important to use superior products should they be developed. On the other hand, the Working Group was concerned companies might be less willing to risk large investments in early research if they faced the prospect of entry of “me too” products offering no significant advance over the original vaccine. However, many of the industry participants interviewed by the Working Group indicated that they would prefer to have multiple suppliers over a winner-takes-all approach. Recognizing that independent research may lead to the development of substantially similar products, another option would be to permit any qualifying vaccines, whether or not superior, that are tendered within a window (*e.g.*, one year) after the approval of the initial Approved Vaccine to be accepted without showing superiority, provided that the second vaccine resulted from independent research and is not simply a generic copy.
19. The Framework Agreement for an early stage vaccine could be in force for a decade or more before a vaccine candidate is presented for final review to the Independent Adjudication Committee. Accordingly, a force majeure provision permitting the Funder to alter the Framework Agreement based upon extraordinary events has been included. The force majeure clause would void or alter the Framework Agreement in the event of major changes to technology, disease epidemiology or the like that make a vaccine either inappropriate or unnecessary or that would require a change in the specifications that would be more burdensome to the Developers. These determinations are subject to judicial review.

<b>24. Indemnification and Insurance:</b>	[TBD]
<b>25. Term and Termination:</b>	<p>The term will begin on the date that [__] Developers have executed the Framework Agreement (the “Effective Date”) and, unless earlier terminated pursuant to Section 22 or this Section 25, continue until the [_____] anniversary of that date, unless a Guarantee and Supply Agreement has been entered into prior to such anniversary in which case the term shall continue until the later of such anniversary and the expiration or earlier termination of the Guarantee and Supply Agreement.</p> <p>Funder shall have the right to terminate the Framework Agreement (a) after the [_____] anniversary of the Effective Date if no Developer has commenced GLP toxicology studies for a product that shows reasonable promise to become an Approved Vaccine, (b) after the [_____] anniversary of the Effective Date if no Developer has commenced clinical trials for a product that shows reasonable promise to become an Approved Vaccine, (c) after the [_____] anniversary of the Effective Date if no Developer has commenced a pivotal clinical trial designed to demonstrate that a product meets the technical specifications and the usability requirements for an Approved Vaccine, (d) after the [_____] anniversary of the Effective Date if no Developer has filed an NDA or other comparable filing for a product that meets the technical specifications and the usability requirements for an Approved Vaccine, and (e) after the [_____] anniversary of the Effective Date if no Developer has entered into a Guarantee and Supply Agreement with respect to an Approved Vaccine.<sup>20</sup></p>
<b>26. Remedies in the Event of Breach:</b>	[TBD]
<b>27. Dispute Resolution:</b>	[Arbitration under AAA rules in NY, NY].
<b>28. Governing Law:</b>	[New York law].
<b>29. Waiver of Immunity:</b>	If the Funder is a sovereign, it will (a) acknowledge that the transactions are subject to private commercial law, and (b) if it has not already done so, waive sovereign immunity.
<b>30. Other Provisions:</b>	Other covenants, terms and provisions as requested by legal counsel to Funder or the Developers.
<b>31. Exhibits:</b>	Guarantee and Supply Agreement.

20. The Funders have the right to terminate the Framework Agreement if certain interim milestones have not been achieved in a timely manner. This provision is included to provide the Funders with an option to end the agreement if the Framework does not appear to be stimulating productive research and development activities. This would permit Funders to pursue other, more promising opportunities.



## Schedule A to model term sheet for Framework Agreement (Malaria)

*Note that these specifications were developed for example purposes only. Further analyses and consultations would be required to arrive at the appropriate specifications for the actual guarantee.*

### I. Technical requirements

#### A. Indication:

1. Prevention of clinical episodes of *Plasmodium falciparum* malaria in infants and young children.

#### B. Target population:

1. 0–4-year-olds in areas of malaria transmission in Africa.

#### C. Efficacy requirements

1. Prevent at least 50% of clinical episodes of malaria due to *P. falciparum*.

#### D. Duration of Protection

1. At least 24 months with no qualitative or quantitative exacerbation of subsequent disease.

#### E. Interference

1. No interference with other pediatric vaccines.

#### F. Regulatory Approval and Quality Control

1. Regulatory approval of a product, with labeling that meets or exceeds the other technical specifications and usability requirements set forth herein, in one or more of Canada, France, Germany, Italy, Japan, [Mexico], Spain, the United Kingdom, the United States, [others] and such other countries with regulatory standards and procedures that are at least equivalent to those in the foregoing countries, as the Independent Adjudication Committee may designate from time to time (each, an “**Approved Regulatory Country**”). The Committee shall have the right to remove any Approved Regulatory Country if its regulatory standards and procedures change after the effective date of the Framework Agreement or the date that it was approved by the Committee, as applicable.

2. Manufacture of product in one or more of Canada, France, Germany, Italy, Japan, [Mexico], Spain, the United Kingdom, the

United States, [others] and such other WHO-qualified countries with regulatory standards and procedures that are at least equivalent to those in the foregoing countries, as the Independent Adjudication Committee may designate from time to time (each, an “**Approved Manufacturing Country**”). The Committee shall have the right to remove any Approved Manufacturing Country if its regulatory standards and procedures change after the effective date of the Framework Agreement or the date that it was approved by the Committee, as applicable.

3. In lieu of one or both of the foregoing requirements, the Committee may rely on an independent, unbiased, expert third party (e.g., the WHO) to determine that the product meets or exceeds the other technical specifications and usability requirements set forth herein, and to ensure that the facilities where, and conditions under which, the product is manufactured are in compliance with Good Manufacturing Practices and other applicable international standards with respect to the manufacture, holding and shipment of vaccines, in each case throughout the term of the Guarantee and Supply Agreement.

### II. Usability requirements

#### A. Dosage:

1. 1 to a maximum of 4 immunizations; EPI schedule preferred.

#### B. Route of immunization:

1. Any, provided conducive to use on a large scale in Eligible Countries as defined in the Guarantee and Supply Agreement.

#### C. Presentation:

1. Multi-dose vials.

#### D. Storage

1. TBD.
2. TBD, e.g. Two years shelf life.

#### E. Safety Requirements

TBD, consistent with existing practices by UNICEF and PAHO.

## **Schedule B to model term sheet for Framework Agreement (Malaria)**

### Standards and Criteria

1. Standards for Addition of New Designated Suppliers  
TBD.
2. Criteria for Termination of Funder's Payment Obligations  
TBD.

## Appendix G

# Model term sheet for Guarantee and Supply Agreement

<b>1. Parties:</b>	Funder(s) and one or more Designated Suppliers. <sup>1</sup>
<b>2. Purpose:</b>	Guarantee that the Designated Supplier(s) receive a specific price <sup>2</sup> for each sale of the Approved Vaccine <sup>3</sup> if the sale qualifies as a Qualified Sale (as defined below) and the Approved Vaccine is purchased for use in an Eligible Country (as defined below), provided that the Designated Supplier commits to supply the Approved Vaccine to Eligible Countries to meet their requirements. <sup>4</sup>
<b>3. Principal Responsibilities of Funder:</b>	Funder will, subject to Sections 7 and 13 below, irrevocably and unconditionally Guarantee that the gross price paid to a Designated Supplier shall be not less than the price set forth in Schedule A (the “ <b>Guaranteed Price</b> ”) for each Qualified Sale of the Approved Vaccine up to the maximum number of sales specified in Schedule A (the “ <b>Approved Maximum</b> ”); <sup>5</sup> provided that (a) the Base Price is not less than the amount specified in Schedule A, and (b) the Approved Vaccine is purchased for use in an Eligible Country. The “ <b>Base Price</b> ” is the amount actually paid, directly or indirectly, by the purchaser of the Approved Vaccine. <sup>6</sup>
<b>4. Principal Responsibilities of Designated Supplier:</b>	The Designated Supplier will (a) use commercially reasonable efforts to create awareness of the availability of the Approved Vaccine in the Eligible Countries in order to meet the public health requirements in the Eligible Countries, <sup>7</sup> (b) [use commercially reasonable efforts to] establish manufacturing capacity for the production of the Approved Vaccine that is sufficient to meet the public health requirements for the Approved Vaccine in the Eligible Countries, <sup>8</sup> (c) obtain and maintain World Health Organization (WHO) prequalification (or any substitute qualification determined by the Committee) for the Approved Vaccine, <sup>9</sup> and those facilities used in its production, as well as any local authorizations and approvals necessary to market and sell the Approved Vaccine in the Eligible Countries, including by complying with all adverse event reporting requirements and providing ongoing evidence of product and production safety and regulatory compliance, (d) provide the Committee with copies of all written communications to or from, including all filings or submissions to, and summaries of all oral communications with, the WHO or any other relevant regulatory agency with respect to the Approved Vaccine, (e) in connection with the marketing, distribution and sale of the Approved Vaccine, comply with the U.S. Foreign Corrupt Practices Act and all other applicable law, <sup>10</sup> (f) provide information as reasonably requested by the Committee from time to time in order to confirm ongoing compliance with the technical specifications and usability requirements set forth in Sections 8 and 9 of the Framework Agreement, (g) agree to be bound by decisions of the Committee acting within the scope of its authority, <sup>11</sup> and (h) continue to supply product to Eligible Countries to meet their requirements as provided in Section 8.

# Notes

1. The Framework and Guarantee Agreement term sheets were designed to accommodate a variety of sponsors, despite the fact that there are substantial differences between governmental and nongovernmental organizations in areas such as funding capacity and ability to contractually commit to the Guarantee Agreement. There were discussions regarding mechanisms for ensuring that sponsors are and remain bound by their financial commitments under the Framework and Guarantee Agreements. In the end, the Working Group concluded that traditional commercial mechanisms for ensuring compliance, such as letters of credit or escrow arrangements, would be unattractive to potential Funders as they would result in increased transaction costs and unnecessarily tie up funds that could be made available for more immediate opportunities. Instead, the Working Group elected to implement a bilateral contract structure, which would permit the Developer to pursue standard contract remedies, such as money damages and specific performance, if the Funders fail to satisfy their financial commitments. The Guarantee Agreement term sheet would permit a single Funder, multiple Funders or a system where a lead Funder parcels out participations to sub-Funders. Some of the potential Funders considered by the Working Group include private foundations, developed country governments and international organizations.
2. The Guarantee Agreement is designed so that price for each Qualified Sale could vary. For example, a higher payment could be made in the early years to permit the Developer to recapture R&D costs and capital investments in manufacturing capacity more rapidly, with lower payments in the later years.
3. The Working Group determined that a price Guarantee, rather than a minimum quantity Guarantee, would be the basis for the incentive. See chapter 4 for an explanation. The pricing structure can be designed to provide substantial insurance against demand risk for prospective vaccine developers so as to yield a net present value of revenue comparable with commercial products even under pessimistic uptake scenarios.
4. Sufficient vaccine must be made available to satisfy the requirements of all Eligible Countries. A Developer could not select a few Eligible Countries where it wishes to offer the vaccine or cease to supply vaccine once the price supplements cease to apply.
5. The Approved Maximum and the Guaranteed Price can be set to yield desired revenue. Price guaranties are on a per treatment basis—such as course of immunization—rather than a per dose basis.
6. A Base Price concept, similar to a co-payment, was introduced to create an incentive to help ensure that qualifying vaccines are not wasted and that payments are not made for unusable vaccines. If countries, or other donors, are required to make a minimum investment in an Approved Vaccine, then there is greater likelihood that appropriate quantities of the vaccine will be procured and that those quantities will be administered. This also provides an additional safeguard that donor funds will not be wasted on a vaccine for which there is no market. Especially for diseases for which the vaccine research is still at an early stage, the technical specifications in the Framework Agreement may be established many years in advance of identifying promising vaccine technology, or, for that matter, the delivery of an Approved Vaccine. Intervening events, such as improvements in sanitation or pesticide use, may render a technically adequate vaccine unnecessary. Similarly, unforeseen characteristics of an Approved Vaccine, such as medically harmless but culturally unacceptable side-effects, which would not have been addressed in the technical specifications, may render an otherwise safe vaccine unsuitable in certain countries. The co-payment requirement helps ensure that the advance market

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- 5. Qualified Sale:** The sale of the Approved Vaccine for use in an Eligible Country shall be deemed a “**Qualified Sale**” if it meets the criteria set forth in Schedule B, as modified from time to time by the Independent Adjudication Committee. In the event of a conflict between Funder and the Designated Supplier over whether a particular sale of the Approved Vaccine satisfies the criteria for a Qualified Sale, the matter shall be referred to the Independent Adjudication Committee, whose decision shall be final and binding on the parties.
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- 6. Eligible Countries:** Each of the countries listed in Schedule C shall be deemed “**Eligible Countries**”). Schedule C may be revised from time to time by the Independent Adjudication Committee in order to (a) add countries whose per capita GDP (as determined by [\_\_\_\_]) is less than [\$\_\_\_\_], or (b) remove countries whose per capita GDP (as determined by [\_\_\_\_]) is greater than [\$\_\_\_\_].
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- 7. Cap on Total Commitment [and Termination of Commitment]:** The total payment obligation of Funder pursuant to the Guarantee and Supply Agreement, including all payments and distributions to the initial Designated Supplier and any additional or replacement Designated Suppliers, shall (a) not exceed, in the aggregate, [\$\_\_\_\_\_] (the “**Maximum Guaranteed Amount**”), and (b) be subject to termination or modification by the Independent Advisory Committee pursuant to Section 22 of the Framework Agreement. [Schedule C of the Framework Agreement sets forth the assumptions underlying the calculation of the Maximum Guaranteed Amount and the criteria for adjusting it if the number of Eligible Countries is materially reduced or a *force majeure* event occurs.]
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- 8. Supply** The Designated Supplier shall supply all requirements of the Approved Vaccines in Eligible Countries during the Funding Term as provided herein and, thereafter, for a period of [10] years, or such longer period as the Designated Supplier may determine (the “**Supply Term**”), at a price not to exceed (a) if the Designated Supplier has received payments for the sale of the Approved Vaccine in Eligible Countries (the “**Gross Sales**”) in amounts, in the aggregate, greater than [\$\_\_\_\_\_] (the “**Minimum Gross Sales Amount**”), then the lesser of [\_\_]% of its fully burdened (without recapture of research and development) costs and expenses to manufacture the Approved Vaccine and [\$\_\_\_\_] per Dose (as defined in Schedule B), and (b) if the Designated Supplier has not received such payments in such amounts, then the per-Dose amount in clause (a) shall be increased by [\_\_]% only until the aggregate Gross Sales for the Approved Vaccine equals the Minimum Gross Sales Amount, whereupon the increase in this clause (b) shall cease to apply.<sup>12</sup>
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- commitment will be used for Approved Vaccines that actually meet the requirements of the Eligible Countries.
7. Although the Designated Supplier has responsibility for generating awareness of the availability of Approved Vaccines in Eligible Countries, the Working Group, as noted above, recognized that the Funders must also share in this responsibility.
  8. It is critical that the Designated Supplier have adequate manufacturing capacity to meet all of the requirements of the Eligible Countries, not just the Approved Maximum amount of product. The Guarantee Agreement requires that the Designated Supplier use commercially reasonable efforts in this regard, but a higher standard, such as best efforts or an absolute obligation, may be preferable in certain circumstances. In addition, as noted below, consideration needs to be given to the contract remedy if the Designated Supplier fails to establish adequate manufacturing capacity, or otherwise to meet its supply requirements, under the Guarantee Agreement, particularly once the Guaranteed Price commitment has been exhausted.
  9. The Working Group recognized that it would be extremely costly to create an Independent Adjudication Committee that was fully capable of evaluating, approving and monitoring the Eligible Vaccines and their ongoing production. Accordingly, the Guarantee Agreement permits the Independent Adjudication Committee to rely on third parties and their procedures, such as the WHO and its prequalification process.
  10. Compliance with the Foreign Corrupt Practices Act was imposed to alleviate concern that illegal payments might be used to generate demand. Obviously, the purpose of the advance market commitment is to generate orders for vaccines that will be used, not to simply to generate orders for vaccines.
  11. The Working Group recognized the tension between the need for certainty in the determinations of the Independent Adjudication Committee and the need for some review. Court review was deemed impractical in most circumstances. Instead, the goal is to create an IAC that would be viewed as independent by all participants in the Framework, but that is subject to review if it exceeds or abuses its authority, and with respect to certain critical decisions such as a decision to alter or terminate the Funder's payment obligation in the face of a force majeure event, as discussed in note 15 below.
  12. The Guarantee Agreement requires that the Designated Supplier continue to make Approved Vaccines available even after the Funding Period expires on a cost-plus basis subject to a cap. If there are multiple Designated Suppliers, the cap will be increased for a limited time for any Designated Supplier that does not receive a certain minimum percentage of the Maximum Guaranteed Amount during the Funding Term, which amount is defined as the Minimum Gross Sales Amount. The increase will cease to be effective, and the cap will return to the predetermined amount, once the Designated Supplier's aggregate sales equal the Minimum Gross Sales Amount. The Minimum Gross Sales Amount is intended to be a rough proxy for a return on the Developer's investment in the Eligible Product, but cannot exceed 100% of the Maximum Guaranteed Amount. For simplicity, the term sheet includes a cost-plus formula, subject to a cap, for determining the ongoing supply price, but it is possible to include more complex hybrid options. For example, a formula could be employed that would allow the Designated Supplier to share in the benefits of reducing the cost of production. In any event, setting the ongoing supply price is a critical component of the advance market commitment.

<b>9. Intellectual Property:</b>	The Designated Supplier shall own all right, title and interest in and to the Approved Vaccine; provided, however, if the Designated Supplier fails to supply Approved Vaccine in the Eligible Countries as required in Section 8 during the Funding Term or the Supply Term and, in any event, within 2 years prior to the expiration of the Supply Term, the Designated Supplier shall grant Funder, or its designee, a non-exclusive, irrevocable, perpetual, license (with the right to sublicense) solely to make, have made, use, sell, offer for sale and import the Approved Vaccine in any Eligible Country, but Funder shall not have rights to any other products and shall have no rights outside the Eligible Countries, except the right to make and have made Approved Vaccine for use in Eligible Countries. The license grant shall be royalty-free, unless the Designated Supplier has not been paid the Minimum Gross Sales Amount, in which case such grant shall be subject to a royalty of [__]% of net sales until such time as the aggregate royalty payments to the Designated Supplier equal the product of (a) [__]%, multiplied by (b) the amount, if any, by which the Minimum Gross Sales Amount exceeds the aggregate Gross Sales of the Approved Vaccine, whereupon such vaccine will be fully paid and no further royalties shall be due. <sup>13</sup>
<b>10. Representation and Warranties:</b>	[TBD]
<b>11. Indemnification:</b>	The Designated Supplier will defend and indemnify the Funder and the members of the Independent Adjudication Committee from all claims and losses arising out of or related to (a) the use of the Approved Vaccine, including claims and losses for physical or mental injury (including death) and (b) infringement or misappropriation of intellectual property. <sup>14</sup>
<b>12. Term:</b>	The Guarantee and Supply Agreement shall begin on the date that the Committee designated the first Approved Vaccine and continue through such time as the Maximum Guaranteed Amount has been paid (the “ <b>Funding Term</b> ”), and, thereafter, until the end of the Supply Term, unless earlier terminated pursuant to Section 13.
<b>13. Termination:</b>	The Guarantee and Supply Agreement may be terminated by either party in the event of a material breach that is not cured within 30 days of notice thereof from the non-breaching party.  In addition, Funder shall have the right to terminate the Guarantee and Supply Agreement (a) with respect to a particular Designated Supplier in the event the Independent Adjudication Committee determines that the Approved Vaccine of that Designated Supplier no longer satisfies the technical specifications and usability requirements set forth in Sections 8 and 9 of the Framework Agreement, or (b) in the event of a <i>force majeure</i> event as determined by the Independent Advisory Committee as set forth in Section 22 of the Framework Agreement. <sup>15</sup>

13. If the Designated Supplier of an Approved Vaccine fails to meet its supply requirements under the Guarantee Agreement, it would be required to grant the Funder, or its designee, a non-exclusive, royalty-free (except as necessary to provide the Designated Supplier with the Minimum Gross Sales Amount, as described above) license to exploit the Approved Vaccine only in Eligible Countries. Although less than ideal, this is intended to make the relevant technology available to the Funder if the Designated Supplier breaches its obligations under the Guarantee Agreement. However, because this provision may not provide much of an incentive not to breach, especially if a Designated Supplier has already received the Maximum Guaranteed Amount and because, even with this license, there could be a disruption of supply, potential Funders may wish to consider other penalties that would disincentivize a Designated Supplier from breaching, such as liquidated damages provisions.
14. Indemnification was deemed to be particularly important to attract qualified members to serve on the Independent Adjudication Committee. It is contemplated that this indemnification would be similar to that which is provided for directors and officers of corporations.
15. A *force majeure* provision permitting the Funder to alter the Guarantee Agreement based upon extraordinary events has been included. The *force majeure* clause would permit the Independent Adjudication Committee to void or alter the Guarantee Agreement in the event of major changes to technology or disease epidemiology that render a vaccine either inappropriate or unnecessary. For example, if advances in pesticides substantially reduced the incidence of malaria in Eligible Countries, then the Funder's financial obligation would be reduced accordingly. As noted in Section 7 of the Guarantee Agreement term sheet, Schedule C would include criteria, such as assumptions underlying the Framework Agreement, to guide the Independent Adjudication Committee in taking any such extraordinary action, which, as noted in the Framework Agreement term sheet, would be subject to review.



<b>14. Addition of New Designated Suppliers:</b>	If the Independent Adjudication Committee determines (by a 2/3 vote of its members and using the standards specified in Schedule B of the Framework Agreement) that a newly developed vaccine is superior to the previously selected Approved Vaccine, whether for certain target populations or epidemiological conditions or otherwise, and the Developer of the newly developed vaccine elects to become a party to the Guarantee Agreement, the Developer of the new vaccine shall be deemed a “Designated Supplier”, the new vaccine shall be deemed an “Approved Vaccine” and the new Designated Supplier shall have the right to compete with the original Designated Supplier to make Qualified Sales of the new Approved Vaccine in the Eligible Countries under the Guarantee Agreement. <sup>16</sup> The addition of new Designated Suppliers and Approved Vaccines shall, in each case, be subject to the cap on Sponsor’s total commitment set forth in Section 7.
<b>15. Remedies in the Event of Breach:</b>	[TBD]
<b>16. Dispute Resolution:</b>	[Arbitration under AAA rules in NY, NY].
<b>17. Governing Law:</b>	[New York law].
<b>18. Waiver of Immunity:</b>	If the Funder is a sovereign, it will (a) acknowledge that the transactions are subject to private commercial law, and (b) waive sovereign immunity.
<b>19. Other Provisions:</b>	Other covenants, terms and provisions as requested by legal counsel to Funder or the Designated Supplier.

16. The Working Group devoted considerable discussion to the question of whether more than one Developer would be permitted to receive payments under the Guarantee Agreement. On the one hand, the Working Group felt that it was important to preserve incentives for product improvements and that it would be important to use superior products should they be developed. On the other hand, the Working Group was concerned companies might be less willing to risk large investments in early research if they faced the prospect of entry of “me too” products offering no significant advance over the original vaccine. However, many of the industry participants interviewed by the Working Group indicated that they would prefer to have multiple suppliers over a winner-takes-all approach. Recognizing that independent research may lead to the development of substantially similar products, another option would be to permit any qualifying vaccines, whether or not superior, that are tendered within a window (*e.g.*, one year) after the approval of the initial Approved Vaccine to be accepted without showing superiority, provided that the second vaccine resulted from independent research and is not simply a generic copy.

## Schedule A to model term sheet for Guarantee and Supply Agreement

### Base Price, Guaranteed Price and Approved Maximum

- A. Base Price. The minimum Base Price shall be an amount not less than [\$\_\_] per Dose (as defined in Schedule B).
- B. Guaranteed Price.
- C. Approved Maximum (quantity of vaccine in Doses).

## Schedule B to model term sheet for Guarantee and Supply Agreement

### Criteria for Qualified Sales

#### A. Buyer Criteria.

1. Buyers Included. Qualified Buyer include (a) UNICEF, (b) WHO, (c) Pan American Health Organization, (d) any individual Eligible Country that is purchasing for the benefit of the public sector or local nonprofits, and (e) and any other buyer approved by the Independent Adjudication Committee.
2. Buyers Excluded. A pharmaceutical company, acting directly or indirectly through one or more intermediaries, shall not qualify as a Qualified Buyer.

#### B. Sales Criteria.

1. Course of Treatment. A single course of treatment, regardless of the number of individual immunizations, required to provide the desired efficacy and duration of protection shall be deemed a single “Dose” and shall constitute a single sale. For example, if 3 immunizations over a period of 2 years are required to achieve the desired efficacy and duration of protection, then the sale of all 3 immunizations, one Dose, shall be required to constitute a Qualified Sale.
2. Bundled Sales. In the event that the Designated Supplier bundles the sale of the Approved Vaccine to a purchaser with the sale or licensing of another product or service of the Designated Supplier or its affiliates, the Designated Supplier shall reasonably assign prices to (allocate revenue amounts between) the Approved Vaccine and such other products or services sold or licensed by the Designated Supplier or its affiliates to the purchaser, in accordance with the terms set forth in Exhibit B1 in order to ensure that the Designated Supplier has attributed a reasonable and equitable portion of that sale to the Approved Vaccine.
3. No Top Up. The Designated Supplier shall not seek or receive any additional compensation or value for the sale of the Approved Vaccine in an Eligible Country other than compensation from the purchaser in the form of the Base Price and the compensation from the Funder under the terms of the

Guarantee and Supply Agreement; provided, however, that the Designated Supplier may seek and receive additional compensation or value if (a) additional Funders are added to the Guarantee and Supply Agreement by amendment, or (b) approved by the Independent Adjudication Committee in writing.

4. Use in an Eligible Country. If the Approved Vaccine is purchased for use in a particular Eligible Country, the Designated Supplier must have a reasonable expectation that the Approved Vaccine will actually be used in such Eligible Country. For purposes of illustrating the foregoing, if UNICEF, as it presently operates, certifies that a country has certain requirements for the Approved Vaccine, then the Designated Supplier will have a reasonable expectation that such requirements of the Approved Vaccine will actually be used in such country.

#### C. Other Criteria.

[TBD]

### **Schedule C to model term sheet for Guarantee and Supply Agreement**

#### Eligible Countries

[Insert e.g. Vaccine Fund–eligible countries.]