Abbott, Tony, 119
Abercrombie, George, 127, 139
access: to market, FDA and, 82; to medical countermeasures, 14, 159–60, 228–29; to pandemic flu vaccines, 40; to raw materials for production, 141, 154, 155. See also access to clinical trial data; access to Tamiflu
access to clinical trial data: as deployment challenge, 207, 208–10, 222–23; on medical countermeasures, 207; for Tamiflu, 184–85, 194–200
access to Tamiflu: by governments, 145–50; in low-income countries, 150–55; political and legal battles over, 137–38; Roche strategies to increase, 155–59
accidental medical countermeasures, 48
acquisition challenges: demand management, 107, 130–32; distribution management, 107–8, 120, 132–33; overview of, 222; regulatory approval, 80, 105
administration of medicine: method of, 54, 61–67; rapid and mass, in UK, 164–65
advertisement of medicines, 109–11
amantadine, 40–41
Anan, Kofi, 153
animal rule of FDA, 17, 102–3, 105, 225
anthrax: inhalational, treatment for, 103; letters laced with, 5–6, 7; vaccine for, 103
antibiotic medication, 37
antigenic drift and antigenic shift, 34
Antiviral Drugs Advisory Committee, 90–93
antiviral medication: for HIV/AIDS, 37, 151; response to influenza viruses and, 37–38; Roche and, 68; supply of, 40–41. See also neuraminidase inhibitors; Relenza; Tamiflu
Aspen Pharmacare, 156–57
attack rates of pandemics, 35
Australia, stockpiling in, 19, 119
avian flu. See H5N1 flu
Bacillus anthrax, 6. See also anthrax
Barclay, Wendy, 214
BARDA. See Biomedical Advanced Research and Development Authority
Barnes, Nigel, 112
Barry, Andrew, 209
Bergstrom, Richard, 216–17
biological dangers: from epidemics, 4–5; from laboratories, 6; molecular vision of life and, 3–4, 235–36; national security and, xi, 1; political rise of global health security and, 4–8; from terrorism, 5–6
Biomedical Advanced Research and Development Authority (BARDA): Centers for Innovation in Advanced Development and Manufacturing, 162; Clinical Studies Network, 105; creation and role of, 17–18, 56, 76, 225; Nonclinical Development Network, 105
Biota Holdings, 44, 46
biotechnology startups, 56
bioterrorism, 5–6, 49–50
BioThrax, 103
bird flu. See H5N1 flu
Bischofberger, Norbert, 61–62, 64
blood-brain barrier, 169
BMJ, 195, 196, 199, 206
British Pharma Group, 112–13
Burns, William, 121
Canada, stockpiling in, 18–19, 119–20
Carpenter, Daniel, 81
Centers for Disease Control and Prevention, US (CDC), 6, 47–48, 187, 203
challenges for medical countermeasures. See acquisition challenges; deployment challenges; development challenges
China, sublicensing agreements in, 156
Chugai pharmaceutical company, 172
Cipla, 153–54
citizens: access to medical countermeasures by, 14; as focus of medical countermeasures, 12; stockpiling of Tamiflu by, 128–30
clinical trials: conflicts of interest in, 188; data from, 184–85, 189–90, 191, 194; as development challenges, 70–71; diversity of persons enrolled in, 166; funding for, 67; for GS4104, 70–76; for medical countermeasures, 176; for pandemic flu, 100–101, 104–5; randomized controlled, 205–6; for Relenza, 91; role of, 79; side effect assessment during, 165–66. See also access to clinical trial data
Coalition for Epidemic Preparedness Innovations, 229
Cochrane Collaboration: clinical trial data and, 191, 194; data requested by, 185; documents sent to Roche by, 192; on evidence base for public health drugs, 209; funding for, 207; on Harvard study, 204; Hayashi and, 190; medicine reviews by, 189; Tamiflu review by, 174–75, 193, 200–203; targeting of regulators by, 196–200
Colman, Peter, 43–44
commercial logic of pharmaceutical defenses, as competing with political logic, 2–3, 12–14, 32–33, 50–51, 223
commercial risks: of compulsory licensing by governments, 148–50, 151–52, 161–62; of drug side effects, 173; mitigation of, 131–32; of regulatory approval, 103–5; in scaling up production, 139–40; of taking product to market, 106; of Tamiflu, 106, 108–16
complications, Tamiflu effect on: claims about, 186, 188–89; clinical trial data on, 188–94; evidence for, 200; Harvard study of, 204; Kaiser study and, 187–88; MUGAS study of, 204–5
compulsory licensing procedures of governments, 146, 148–50, 151–52, 161–62
Comstock, Amy, 124
conflicts of interest: appearance of, 230; in clinical trials, 188; of governments, 183; of Jefferson, 203; of MUGAS, 205; of Rumsfeld, 124, 125; of WHO, 196
Consumer Project on Technology, 147–48
corporations, stockpiling of Tamiflu by, 126–28
cost-benefit analysis of medicines, 106, 111–14, 117
costs of maintaining status quo, 228–29
counterfeit Tamiflu, 129–30
Crome, Renata, 70
Cyanokit, 102–3
data access campaign: regulators as target of, 196–200; Tamiflu and, 194–96
Davis, Sally, 214
Defense, US Department of: Defense Advanced Research Projects Agency, 61; laboratory of, and anthrax, 6; medical countermeasures and, 11, 12; Tamiflu stockpile for, 123, 125–26
demand management challenges, 107, 130–32, 222
development challenges: economic, 33, 52–53; engagement by large pharmaceutical companies, 218; late-stage work, 54–55, 75–76; overview of, 221–22; scientific, 33, 51–52. See also clinical trials
Dick, Mathias, 108, 109
direct-to-consumer marketing, 109–11
distribution management challenges, 107–8, 120, 132–33, 222
division of labor, “upstream” and “downstream,” 74
Doha Declaration, 151–52, 153
dosage, safe, establishment of, 71
drug development: conventional process of, 31–32, 55; emerging pattern of, 54–55; “holy grail” of, 84; late-stage work of, 55–56, 75–76, 221–22. See also development challenges
“drug serendipity,” 66
Ebola, 5, 221, 227
economic challenges to development, 33, 52–53, 221
efficacy: assessment of, 71–72; of medical countermeasures, 19–20; of neuraminidase inhibitors for pandemic flu, 100–101; of Relenza, 91–93. See also complications, Tamiflu effect on
Elashoff, Mike, 91–93, 94–96
EMA. See European Medicines Agency

emergency use authorization (EUA), 179–82
encephalopathy, influenza-associated, 171
epidemic of epidemics, 1
EU. See European Union

EUA (emergency use authorization), 179–82
Europe, stockpiling in, 121–22. See also
European Union
European Centre for Disease Prevention and Control, 49, 215–16
European Medicines Agency (EMA): on
access to clinical trial data, 207;
antiobesity drug data and, 196–98;
Cochrane Collaboration and, 198; on
effect of Tamiflu on complications, 192;
Tamiflu approval and, 86, 87, 88, 99
European Ombudsman, 197, 199
European Union (EU): approval of Tamiflu
in, 85–89, 99–100; direct-to-consumer
marketing in, 110; Health Security Com-
mittee, 7; health security framework for,
181; medical countermeasures and, 10,
19; regulatory approval process in, 105;
stockpiling strategy for, 122–23
failures of pharmaceutical products, 51
flu, types of, 23. See also H1N1 flu pandemic;
H5N1 flu; pandemic flu; seasonal flu
Flyer, Paul, 100–101
Food and Drug Administration, US (FDA):
animal rule of, 17, 102–3, 105, 225;
Cochrane Collaboration and, 199; direct-
to-consumer marketing and, 110; EUA by,
179–80; Relenza and, 90, 93–99; reported
side effects and, 170–71; Tamiflu and,
82–84, 192–93
funding: for clinical trials, 67; from
governments, 55, 61, 75, 218–19, 225;
for research, 52; for Strategic National
Stockpile, 15, 16
GG167 molecule, 52
Gilead Sciences: Bischofberger and, 61–62;
board for, 58–60; computer technology of,
64–65; discovery of GS4104 by, 65–66;
first decade of, 60–61; government agree-
ments of, 61; influenza agents of, 62–63;
origins of name of, 57; patents of, 66, 69;
Roche and, 68–70, 138, 143–45; royalties
paid to, 145; Rumsfeld and, 123–25;
scientists for, 57–58. See also
GS4104
Glaxo Wellcome, 46–47, 70, 73, 94, 98.
See also Relenza
global health security: definition of, 7;
medical countermeasure enterprise for,
226–31; political rise of, 4–8
Global Health Security Agenda, 7–8
Global Health Security Initiative, 7
global justice issues, 157
Godlee, Fiona, 195, 214
Goldacre, Ben, 192, 195, 201, 209
governments: conflicts of interest of,
183; cost-benefit analysis of medicines
by, 111–14; demand and distribution
management by, 107–8; funding from,
1, 55, 75, 218–19, 225; health security
and, 4–8; implementation of vision by,
12–19; investment in research by, 52;
medical countermeasure development
and, 218–19; pandemic preparation by,
36–41; partnerships with pharmaceutical
companies, 55, 61, 75, 230–31; quest of
medical countermeasures by, 8–12; role
of, 212. See also regulatory approval pro-
cess; stockpiling of medicines
GS4104: clinical trials for, 70–76; discovery
of, 61–67, 65–67; late-stage development
of, 67–68; licensing to Roche of, 68; name
for, 73–74. See also Tamiflu
H1N1 flu pandemics: media coverage of, 22;
of 1918, 34; stockpile deployment during,
15; swine flu origin of, 5; of 2009–2010,
184, 185–86, 230; in UK, 164–65
H5N1 flu: origins of, 4–5; outbreak of, 35;
pandemic scare, 22; reappearance of,
35–36; stockpiling and, 119–23; Tamiflu
and, 107, 116–19
H7N7 virus, 116
H7N9 virus, 5, 220–21
Hama, Rokuro, 168, 169–70, 172, 175,
188
Hamied, Yusuf, 153–54
Hamilton, John, 93
Harvard study, 204
Hayashi, Keiji, 188–89, 190
Hayden, Fred, 187, 191
Health and Human Services, US Department
of (HHS), 12, 177, 180–81
health security: commercial potential in area of, 32–33; concerns about, and approval of Relenza, 98–100; definition of, 7; double-faced nature of threats to, 150; global, 4–8, 226–31; perceptions of pharmaceutical products and, 130; resistance to notion of, 8; scholarly work on, 20; uncertainty of threats to, 49–50, 52–53
hemagglutinin, 42
Heneghan, Carl, 213
Hetero pharmaceutical company, 156
HHS (Health and Human Services, US Department of), 12, 177, 180–81
Hirota, Yoshio, 172
Hirst, George, 42
HIV/AIDS: antiviral medications for, 37, 151; Cipla and medications for, 153; global justice issues and, 157; global spread of, 4
hosts for influenza viruses, 33
Houseago, Harry, 165
Humer, Franz, 68, 69, 70, 115, 144
Hurley, Terry, 146
Iacuzio, Dominick, 140–41
India, pharmaceutical companies in, 153–54
Indonesia, H5N1 virus samples of, 229
influenza viruses: characteristics of, 33–34; encephalopathy associated with, 171; human body response to, 37–38; neuropsychiatric adverse events associated with, 169, 173–74. See also specific viruses, such as H5N1 flu
inhalation drug for flu, 62
Institute of Medicine, 10
intellectual property, 148, 151–53, 161–62, 222. See also patents
Internet sales of Tamiflu, 128–30
Interscience Conference on Antimicrobial Agents and Chemotherapy, 61–62
investment in scientific research, 52
Jack, Andrew, 130, 168–69
Japan: alerts about Tamiflu in, 172, 173; approval of Tamiflu in, 84–85; as consumer of Tamiflu, 166–67; deaths in, 168–70, 171, 175, 183; health security framework for, 181–82; reimbursement for Tamiflu in, 115; side effects reported in, 167–68, 170
Jefferson, Thomas, 190–91, 198–99, 203, 207
Kaiser, Laurent, study by, 187–88, 189
Kim, Choung, 62–63, 64
Kucinich, Dennis, 146
Kyprianou, Markos, 122
laboratories, accidental releases from, 6
Lapre, David, 141, 142, 145, 161
late-stage development challenges, 54–55, 75–76, 221–22
Laver, Graeme, 43, 44, 46, 64, 66
Leavitt, Michael, 120–21, 149
legal framework for medical countermeasures in US: EUA, 179–82; overview of, 16–17, 225; tort liability protection, 177–79
Levaquin, 103
liability for harm, financial and legal, 175–83, 222
life, molecular vision of, 3–4, 235–36
life-course approach, 24–28
Lipsitch, Marc, 204
logistical mass distribution systems, 107–8, 120, 132–33, 222
low- and middle-income countries, access to Tamiflu by, 150–55, 157
"magic bullet" policy solutions, 3, 27, 212, 224
market: constituting artificially, 218–19; diseases with dual markets, 219–20; FDA and access to, 82; logic of, as completing with political logic, 2–3, 12–14, 32–33, 50–51, 223; for medical countermeasures, 49–51; for pandemic flu medications, 32; for seasonal flu medications, 45–48; taking product to, 106. See also commercial risks
Martin, John, 69, 123–24
Mathys, Patrick, 215
McConway, Kevin, 202–3
media coverage, 1, 22, 123, 128–29, 140, 141
medical countermeasure enterprise: global, 226–31; in US, 3, 15–19, 224–26
medical countermeasures: access to, 14, 159–60; access to data on, 194–200, 207, 208–10; accidental, 48–49; broad-spectrum, 220; definitions of, xi, 10; demand for, 130–32; efficacy of, 19–20; as expansion of government ambition, 11–12; as interdisciplinary policy space,
Index 259

11; knowledge of issues related to, 19–20; market for, 49–51; policy challenges of, 3; proactive development of, 1–2, 9–10; quest for new, 8–10; regulatory approval process for, 17, 80, 101–3; Roche and, 217–18; security context for, 211, 223, 231–32; societal and political role for, 10–11; stakeholders in, 208; supported by BARDA, 105. See also acquisition challenges; deployment challenges; development challenges; Tamiflu

Menlo Ventures, 56–57

Middle East respiratory syndrome (MERS), 5, 220

military, as focus of medical countermeasures, 11, 12, 123, 125–26

Milligan, John F., 144

molar model of life, 235

molecular biology, 31–32, 233–34, 236

molecular vision of life, 3–4, 235–36

Montgomery, DuBose, 58

Moore, Gordon, 58

Morishima, Tsuneo, 172

mortality, effect of Tamiflu on, 206

Multiparty Group for Advice on Science (MUGAS), 204–5

National Institute for Clinical Excellence (NICE, UK), 112–13

national security. See biological dangers; health security; security context for medical countermeasures; security policy

neuraminidase inhibitors: birth of, 31, 42–45; in capsule form, 61–67. See also Relenza; Tamiflu

neuropsychiatric side effects. See side effects of Tamiflu

Nguyen-Van-Tam, Jonathan, 206, 213

NICE (National Institute for Clinical Excellence, UK), 112–13

Nicoll, Angus, 49, 215–16

“Ode to Tamiflu” (Houseago), 165

Oligogen, 56–57. See also Gilead Sciences

Openshaw, Peter, 202

oseltamivir. See Tamiflu

Palmer, James, 94, 98

pandemic flu: approval of Relenza and threat of, 79–80, 98–99; approval of Tamiflu and threat of, 99–100; attack rates of, 35; business continuity plans for, 126–28; clinical trials for, 100–101, 104–5; definition of, 23, 33; efficacy of neuraminidase inhibitors for, 100–101; government continuity plans for, 123, 125–26; market for medication for, 32; preparation for, 37–41, 114–16; socioeconomic disruption of, 9, 35, 36, 41; Tamiflu and insurance policy approach to, 117–19; threat of, 33–37, 49. See also H1N1 flu pandemic

pandemics, biological and social, 214

patents: challenge of, 222; of Gilead Sciences, 66, 69; in India, 153; overriding of, 138–39, 147, 148, 149; pharmaceutical companies and protection of, 148–49; for Tamiflu, 211; as time limited, 81

pharmaceutical companies: in India, 55, 61, 75, 230–31; patents of, 148–49; priorities of, 2, 13–14, 32–33; publication of studies and, 195; regulatory approval stage and, 81, 103–4; reputation of, 230; risks for, 13; small compared to large, 54–55, 61, 74–75; specialized regime for, in US, 3, 15–19, 224–26. See also access to clinical trial data; clinical trials; commercial risks; specific companies, such as Roche

pharmaceutical defenses: access to, 9; complexity of studying, 20–21; overview of, 1–2; in security policy, xi–xii. See also medical countermeasures; Tamiflu

pharmaceuticalization of security policy, 3, 233, 235

pharmaceuticals in society, scholarly work on, 20

pharmacovigilance, 166

phase 1 clinical trials, 71

phase 2 clinical trials, 72

phase 3 clinical trials, 72–73

pneumonic plague, 103

political logic: of pharmaceutical defenses, as competing with commercial logic, 2–3, 12–14, 32–33, 50–51, 223; of stockpiling, 213–17

Portugal and Tamiflu, 87–88

Post-Pandemic Review of Anti-Influenza Drug Effectiveness (PRIDE), 206
power battles: between regulators and Cochrane, 196–200; between Roche and Cochrane, 191–94, 207; between Roche and governments, 145–50
preparation for pandemic flu, 37–41. See also stockpiling of medicines and vaccines production of Tamiflu: difficulty of, 140–41, 154–55; rapid scale up of, 138, 139–43, 160, 162, 222
Project BioShield, 16, 18, 179, 181, 219 publication bias, 195
Public Health Emergency Medical Countermeasures Enterprise, 11–12
public health interventions, traditional, 9, 36–37, 41
pyridostigmine bromide, 102
"rational" drug design, 66–67
ravixabacumab, 103
Reddy, David, 114, 121, 141, 155, 158, 186, 191
regulators, as target of data access campaign, 196–200
regulatory approval process: challenges of, 80, 105, 222; in EU, 86–87; EUA and, 179–82; for medical countermeasures, 17, 80, 101–3; overview of, 79, 80–81, 103–4
regulatory approval process for Relenza: Antiviral Drugs Advisory Committee and, 90–93; FDA and, 93–99; overview of, 90; pandemic flu threat and, 79–80, 98–99
regulatory approval process for Tamiflu: conclusions on issue of effect on complications, 192–93; in Europe, 85–89; at FDA, 82–84; in Japan, 84–85; overview of, 81–82, 89–90; pandemic flu threat and, 99–100; Relenza backstory and, 95–97
Relenza (zanamivir): Antiviral Drugs Advisory Committee and, 90–93; clinical trials for, 91; commercial drug development process for, 32; development of, 31, 51, 52; FDA and, 93–99; marketing of, 110; method of administration of, 62, 63; naming of, 48; NICE and, 112–13; pandemic flu threat and, 79–80, 98–101; sales of, 111, 113; Tamiflu compared to, 54–55, 74. See also regulatory approval process for Relenza
Rex, John, 51
Rice, Condoleezza, 59–60
rimantadine, 40–41
Riordan, Michael, 56–57, 58, 60–61, 64, 65. See also Gilead Sciences
risk: for complications from flu, 48; modeling and communicating, 8–9. See also commercial risks
Roche: clinical trial data and, 191–92, 193–94, 196; clinical trials for GS4104 and, 70–76; Cochrane and, 201–2; Gilead Sciences partnership of, 54–55, 67–70, 138, 143–45; government pressure on, 145–50; international stockpile and, 157–59; lessons from experiences with Tamiflu, 217–21; pandemic preparedness plan of, 127; pressures on, 137–38, 155; release of data by, 198, 199; reserve program of, 127–28, 159; response to Cochrane fallout by, 203–8; scaling up of production by, 139–43; studies of side effects sponsored by, 173–75; sublicensing agreements of, 155–57. See also Tamiflu
Rose, Nikolas, 235
Rumsfeld, Donald, 58–60, 123–25
Russian flu, 34
safety, assessment of, 72–73
Sampaio, Cristina, 87, 89
Sanders, Bernie, 147
SARS (severe acute respiratory syndrome), 4, 6 scaling up production, 138, 139–43, 160, 162, 222
Schmidt, Benno, 58
Schneider, Reto, 70
Schultz, George P., 59
Schumer, Charles E., 147
scientific challenges to development, 33, 51–52, 221
Seaborg, Glenn, 57
seasonal flu: commercial lure of market for, 45–48; definition of, 23, 32; in Japan, 85; vaccines against, 38–39
security context for medical countermeasures, 211, 223, 231–32
security policy: pharmaceutical defenses in, xi–xii; pharmaceuticalization of, 3, 233, 235
severe acute respiratory syndrome (SARS), 4, 6
Sherman, Susan, 180
table effects: assessment of, 165–66; harmful, liability for, 175–82
side effects of Tamiflu: Cochrane review on, 200–201; concerns about, 163–64; FDA and, 170–72; infrequent or rare, 174–75; in Japan, 167–70; Japanese studies of, 172–73; Roche studies of, 173–75; in UK, 164–65
Singapore, regional stockpile in, 123
social lives of medicines, 24, 223–24
socioeconomic disruption of flu pandemics, 9, 35, 36, 41
Soman nerve agent poisoning, 102
Southern Hemisphere, clinical trials in, 73
Spanish flu, 34
Sprenger, Marc, 215–16
Stanton, John, 123, 125, 126
star anise, 141, 154, 155
Strategic National Stockpile (SNS, US), 15–16, 22, 115, 120, 225
surge production, 138, 139–43, 160, 162, 222
surveillance systems, 9, 166
Swaminathan, Swami, 64
swine flu. See H1N1 flu pandemic
Switzerland: cost-benefit analysis of medicines in, 111; marketing in, 109–10; regulatory approval of Tamiflu in, 81–82
symptom “rebound,” 92
Szostak, Jack, 58
Tamiflu: claims about benefits of, 186, 188–89; as competitor to Relenza, 54–55; deployment of, 22–23; development of, 31; EUA for, 179, 180; global demand for, 107, 116–19; H1N1 flu pandemic and, 185–88; learning from life of, 24–28, 211; marketing of, 110–11; naming of, 73–74; NICE and, 113; obstacles to commercial success of, 106, 108–16; overview of, xi–xii, 21; for pandemic flu, 114–16; patent for, 211; for pediatric use, 84; prophylactic use of, 83, 84, 113, 158–59; sales of, 111, 113, 132, 145; shelf life for, 212–13; stockpiling of, 21, 119–23, 178, 213–17; as subject of research, 21–22; supply network for, 160–61; supply of, 137; surge production of, 138, 139–43, 160, 162. See also access to Tamiflu; GS4104; production of Tamiflu; regulatory approval process for Tamiflu; side effects of Tamiflu
Tashiro, Masato, 169
technical constraints in scaling up production, 140–41
tort liability protection, 177–79
Trade- Related Aspects of Intellectual Property Rights (TRIPS), 151–52, 153
Troy, Tevi, 126–27
trust issues, 14, 182, 183, 201, 230–31
United Kingdom (UK): cost-benefit analysis of medicines in, 112; side effect of Tamiflu in, 164–65; stockpiling in, 19
United Nations Security Council and HIV/AIDS, 4
United States (US): costs of maintaining status quo to, 228–29; medical countermeasure enterprise in, 3, 15–19, 224–26; political pressure on Roche from, 146–50; stockpiling in, 15–16, 18–19, 22, 115, 120–21, 224–25. See also legal framework for medical countermeasures in US; specific agencies
vaccines, 16, 38–40, 103. See also stockpiling of medicines and vaccines
Varmus, Harold, 58
venture capital, 56
viruses, targeting of, 37–38. See also specific viruses, such as H5N1 flu
von Itzstein, Mark, 44, 62
Ward, Penny, 70, 71–72, 84–85, 87–88, 144, 174, 186
Wilson, Gayle, 59
World Health Organization (WHO): on global health security, 7; guidance on pandemic flu issued by, 118–19, 196; H1N1 pandemic and, 5; R&D Blueprint of, 227; Tamiflu and, 21, 157–59
World Trade Organization (WTO), 151–52
Yokota, Shunpei, 172
zanamivir. See Relenza
Zika virus, 5, 221
This page intentionally left blank