Cambridge University Press & Assessment 978-1-009-39698-1 — Accelerating Diagnostics in a Time of Crisis Steven C. Schachter, Wade E. Bolton Index More Information

Index

Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV), 44 ACME POCT verification protocol, 159 analytical studies (RADx), 93-94 antibodies, neutralizing, 40 antibody test, 239 antigen tests defined, 127, 239 impact of variants, 178 Regulatory Core, 198-199 sample type, 128 barriers (COVID-19 test commercialization) digital infrastructure, 232-234 payment policies, 228-230 point-of-care (POC) assays, 227-228 privacy and liability issues, 230-231 regional guidance and messaging, 231-232 biobanking clinical samples, 162 RADx, 184-185 variant vendor selection, 185 burnout (frontline workers), 255-256 Centers of Disease Control and Prevention (CDC), 24 China assessment of early infectivity, 10 disease progression, 11-12 first cases, 6-10 first COVID-19 analysis, 14 information censure, 9 novel coronavirus announcement, 9 sequencing laboratory closure, 10 Wuhan lockdown, 11 classification, COVID-19 variant

GISAID, 175 Nextstrain, 175 Pango, 175 WHO convention, 176 Clinical Review Committee (CRC) participants, 131 process, 131-133 use-related risk analysis, 121 clinical studies (RADx), 94 CoLab, 77 commercialization of test assays, core functions barrier identification, 227-232 business development, 224 - 225business support, 224 education, 224 at-home testing pricing, 223-224 internal capabilities assessment, 213-214 market education, 226-227 market intelligence, 225 market research, 214-215 quantitative database, 215-216 stakeholder findings, 216-222 contact tracing, 17, 243-244 COVID-19 dashboard (WHO), 25 - 26COVID-19 Genomics UK (COG-UK), 172 COVID-19 pandemic. see also SARS-ĈoV-2 comprehensive response roadmap, 268 high-level lessons learned, 269 quality management system (QMS), 113-114 quality management system (QMS) reprioritization, 117 roadmap highlights, 264-268

test development quality, 114-115 vaccine platform features, 42 COVID-19 pandemic, early detection disease progression, 11-12, 14 early clinical intervention methods, 61 first cases, 6-10 health emergency declaration, 12 link to SARS-CoV and MERS-CoV, 9 outbreak, 6 viral infectivity assessment, 10 viral pathogen sequencing, 10 COVID-19 pandemic, management challenges, 25 main strategy, 23 testing utility, 25 COVID-19 pandemic, mitigation strategies challenges, 236 contact tracing, 243-244 importance of flattening infection curve, 246 Isolat model, 240-242 KN95 masks, 242-243 pooled testing, 245-246 **ROSALIND** Diagnostic Monitoring (DxM), 239-240 testing adoption support, 237-239 testing public policy, 246-248 vaccination, 243 COVID-19 pandemic, response areas to improve on, 258 - 260cloud-based infrastructure tools, 76-77 comprehensive response roadmap, 268

Cambridge University Press & Assessment 978-1-009-39698-1 – Accelerating Diagnostics in a Time of Crisis Steven C. Schachter, Wade E. Bolton Index More Information

contact tracing, 17	epidemiological and clinical	deep dive team (RADx)
Dondomic	endiacteristics, 22	applicant contact point, 82
Pandenne Dronaradnasa 19	formate 22	components, 81
data and communications	at home testing problems 22	fast commonsistince, 82
cocurity 77	implementation and	
security, //	management 22	plan, 82
global, 14–17	information overload 21, 22	proposal criteria, 82
giobal community	initial lack of 12	RFP market research, 84
Clabal Health Security	militar lack 01, 12	Defense Production Act (DPA)
(CLIS) In day 19	machine learning, 25	ratings, 94–95
(GHS) Index, 18	nanobeaus technique, 25	Deployment Core
global preparedness lack, 18	number of cases data	additional resources, 93
tachnology 14	WHO recommendations 22	manufacturing, 92–93
IDDDD arman nan art 26, 27	COVID 10 pag domin tosting	process development, 88
lessons learned 27, 28	coviD-19 pandemic testing	procurement, 91–92
Den Louis Orenzisht	adoption support	resources supplied, 88–90
Pandemic Oversight	goals of, 237	role of, 88
Committee, 18	at-nome testing, 237	supply chain, 91
Pandemic Response	My COVID Toolkit, 239	test reimbursement
Accountability Committee	Project N95, 238	support, 93
(PRAC), 18	when to test (website),	Deployment Core, core
public health and social	23/-238	resources
measures (PHSM), 18	COVID-19 Response and	project management, 91
Public Health Emergency	Pandemic	quality management, 91
Medical Countermeasures	Preparedness, 18	regulatory affairs, 91
Enterprise, 18	COVID-19 variants. see also	design history file (DHF), 117
Rapid Acceleration of	Variant Task Force (VTF)	design review process (RADx),
Diagnostics (RADx)	antigen test impact, 178	100-101
initiative, 1/-18	classification, 175–176	device history record
research and development	molecular test impact,	(DHR), 112
prioritization, 12–14	176–178	device master record
roadmap, 7	pre-variant context, 173–174	(DMR), 117
social distancing and	public awareness, 1/4–1/5	diagnostic test assay clinical
personal protective	sequencing methods, 171	verification
equipment, 17	surveillance, 166	inclusion and exclusion
summary, 268–273	timeline, 166	parameters, 161
COVID-19 pandemic, social	cross-reactivity studies,	partnerships, 160
impact	Emergency Use	rural mobile units, 161
areas to improve on,	Authorization, 201	site staffing and training,
258-260		160–161
direct impacts, 250–253	database organization (COVID	staff turnover planning, 161
divided positions on masks,	clinical testing)	diagnostic test assay clinical
testing, and vaccines,	collection and results, 163	verification data collection
256-257	consent forms, 162	clinical samples, 162
indirect impacts, 253–254	demographic	database organization,
long COVID, 257	characteristics, 163	162–164
mental health, 254–256	inclusion/exclusion	diagnostic test assay
misinformation dangers,	form, 162	commercialization
256	participant reimbursement,	(COVID-19)
positive consequences of,	163–164	core functions, 211–234
257-258	participant status, 163	RADx, 211
timeline roadmap, 250	protocol deviations and	diagnostic test assay design
COVID-19 pandemic,	adverse events, 163	across changing pandemic
surveillance	server back-up	landscape, 140
COVID-19 dashboard	procedure, 164	biosafety issues, 129
(WHO), 25–26	standard of care test, 163	considerations, 133

Index

275

Cambridge University Press & Assessment 978-1-009-39698-1 — Accelerating Diagnostics in a Time of Crisis Steven C. Schachter, Wade E. Bolton Index More Information

276	Index	
276	Index	

documentation (COVID-19

laboratory testing)

results section, 159

background section, 158

diagnostic test assay (cont.) controls, 136 delayed analysis, 129 direct detection assays, 135-136 hardware, 136 instrumentation, 136 nucleic acid amplification test (NAAT), 133-135 optimization, 136-137 over-the-counter (OTC) assay, 128 point-of-care (POC) assay, 127-128 preclinical testing, 139-140 result timing, 129 sample collector, 128-129 test performance, 137-138 test target audience, 129-131 diagnostic test assay laboratory verification ACME POCT verification protocol, 159 documentation, 158-159 inactivated virus in BSL2 laboratory, 148-149 live SARS-CoV-2 in BSL3 laboratory, 145-148 roadmap, 143 sensitivity studies, 149-153 timeline and steps, 145 variant samples for ITAP, 156 - 158variant studies, 149 diagnostic test classification antigen tests, 127 molecular tests, 127 diagnostic test classification (COVID-19) antibody test, 239 antigen tests, 127, 239 molecular tests, 127, 239 diagnostic tests (COVID-19) roadmap, 126 in vitro diagnostics (IVD), 125 digital infrastructure (testing) changing pandemic landscape, 232-233 RADx reporting solutions, 234 result reporting, 233-234 traditional model, 232 direct detection assays, 135-136

study purpose section, 158 test method section, 158-159 variant pool section, 158 early detection (COVID-19) disease progression, 11-12, 14 early clinical intervention methods, 61 first cases, 6-10 health emergency declaration, 12 link to SARS-CoV and MERS-CoV, 9 outbreak, 6 viral infectivity assessment, 10 viral pathogen sequencing, 10 Emergency Use Authorization (EUA) application, 199 clinical evaluation, 205-206 cross-reactivity studies, 201 flex studies, 206 inclusivity, 200 interference testing, 201 laboratory-developed test (LDT), 207 limit of detection (LOD), 200, 206 post-market commitments, 206 - 207process evolution, 207-208 Regulatory Core, 197-198 right-of-reference (ROR), 207-208 stability, 201-204 usability studies, 206 environmental racism, 252 epitope mapping, 185-186 Europe, COVID-19 introduction, 14-16 failure modes and effects (FMEA), 121 fault tree analysis (FTA), 121 flex studies, 206 Food and Drug Administration (FDA), 196

GAITS, 77 GenBank, 171 gender inequalities and COVID-19, 253 Global Health Security (GHS) Index, 18 Global Initiative on Sharing All Influenza Data (GISAID), 172, 175 health-care system crisis global nature of, 19 medical supply chain, 19 heat map goal of, 97 key, 99 herd immunity, 41 horseshoe bats, 19-20 humoral immune response, 39-40 immunology, defined, 31 immunology, SARS-CoV-2 adaptive immune response, 39-40 entry into cell, 31-34 herd immunity, 41 innate infection immunity as double-edged sword, 36-38 innate infection response, 35-36 overview of normal system, 35 roadmap, 32 several components to, 31 in vitro diagnostics (IVD), 125 Independent Test Assessment Program (ITAP), 95-96 innate lymphoid cell (ILC), 38 interference testing, 201 interferons (IFNs) defined, 35 Type I, 36 ISO 13485, 106–107, 117 ISO 14971:2019, 107 Isolat model (IDSS COVID-19 Collaboration), 240-242 ISO/TR 24971:2020 Annex H, 107 ITAP lot-to-lot variability, 158 reason for, 156 test performance against delta variant, 157 variant testing, 157

		Index	277
KN95 masks, 53–54, 242–243,	Mobile and At-home	Mount Sinai Beth Israel	(MSBI)
256–257	Reporting through	medical center staf	f

laboratory types (testing) BSL2, 148-149 BSL2 and BSL3 comparison, 147 BSL3, 145-148 laboratory-developed test (LDT), 207 LAMP tests, 135 limit of detection (LOD) **Emergency Use** Authorization, 200 performance, 206 logistical challenges (RADx), 97 long COVID, 257 manufacturing (Deployment Core) additional resources, 92-93 quality management system (QMS), 112 masked palm civets, 19-20 mental health and COVID-19 child, 254-255 frontline workers burnout, 255-256 problem amplification, 254 widespread demographics, 255 MERS-CoV-2, 19-20 misinformation dangers (COVID-19), 256 MisinfoRx toolkit (website), 256 mitigation strategies (COVID-19) challenges, 236 contact tracing, 243-244 importance of flattening infection curve, 246 Isolat model, 240-242 KN95 masks, 242-243 pooled testing, 245-246 ROSALIND Diagnostic Monitoring (DxM), 239-240 testing adoption support, 237-239 testing public policy, 246-248 vaccination, 243

Standards (MARS), 234 molecular tests defined, 127, 239 impact of variants, 176-178 Regulatory Core, 198 sample type, 128 Mount Sinai Beth Israel (MSBI) medical center clinical management emergency department case study, 54-55 challenges, 56 early testing and diagnosis, 55 facility modification, 55-56 mortality rate, 57-58 population morale and communication, 58 staff support, 56 telemedicine, 56-57 Mount Sinai Beth Israel (MSBI) medical center clinical management roadmap personal protective equipment (PPE), 53-54 pre-COVID-19 pandemic, 50 - 52summary, 51 surge response, emergency management, 52-53 testing evolution, 58 Mount Sinai Beth Israel (MSBI) medical center hospital medicine 1918 influenza epidemic, 73 case study, 63 decanting hospital efforts, 64 - 65external morale, 65 internal morale, 65 operational changes, 63-64 subsequent pandemic waves, 65-66 vaccine development, 66-68 Mount Sinai Beth Israel (MSBI) medical center intensive care unit case study, 58-59 early clinical intervention methods, 61 patient surge, 59-60 staff deployment, 61

support initiatives announcement schedules, 62 donation management, 63 recharge room and fitness center, 63 town halls, 62-63 work from home, 63 Mount Sinai Beth Israel (MSBI) medical center therapeutic interventions non-therapeutic, 62 stress and mistrust, 61-62 mutational order approach, 12 My COVID Toolkit, 239 nanobeads technique, 23 National Institute of Biomedical Imaging and Bioengineering (NIBIB), 74 National Institutes of Health (NIH) 2020 public-private vaccine partnership, 44 National Institute of Biomedical Imaging and Bioengineering (NIBIB), 74 NK cells, 38 nucleic acid amplification test (NAAT) LAMP tests, 135 PCR based, 133-135 severity score calculations, 181 optimization (assay) turnaround time, 137 workflow, 137 organizational size, quality management system (QMS), 105-106 over-the-counter (OTC) assay, 128 Oxford-AstraZeneca vaccine development, 44 Pandemic Oversight Committee, 18 Pandemic Response Accountability Committee (PRAC), 18

pathogen-associated molecular pattern (PAMP), 36 Cambridge University Press & Assessment 978-1-009-39698-1 — Accelerating Diagnostics in a Time of Crisis Steven C. Schachter, Wade E. Bolton Index More Information

278 Index

patient zero, 12 pattern recognition receptor (PPR), 35 personal protective equipment (PPE) KN95 masks, 242-243 Mount Sinai Beth Israel (MSBI) medical center, 53 - 54Project N95, 238 response to COVID-19, 17 point-of-care (POC) assays, 127-128, 227-228 Point-of-Care Technologies Research Network (POCTRN), 74-76 pooled testing, 245-246 preclinical testing comparator selection, 139 reason for, 139 sample selection, 139-140 preliminary hazard analysis (PHA), 121 procurement (Deployment Core), 91-92 product development process (PDP), 110 project management (Deployment Core), 91 public health and social measures (PHSM), 18 Public Health Emergency Medical Countermeasures Enterprise, 18 public health emergency of international concern (PHEIC), 12 quality management (Deployment Core), 91 quality management system (QMS) best practices, 115-116 COVID-19 pandemic test development quality, 114-115 defined, 103 development and testing, 110 - 112documentation impact, 113 in early development, 110 manufacturing, 112 organizational size, 105-106 product development process (PDP), 110

reprioritization of standards, 117 supplier management, 117-121 quality management system (QMS), regulations and standards 21 CFR 820, 106-107 ISO 13485, 106-107 similarities in, 107 racial and ethnic group impact (COVID-19), 250 raccoon dogs, 19-20 Rapid Acceleration of Diagnostics (RADx) initiative. see also United States analytical studies, 93-94 biobanking, 184-185 Clinical Review Committee (CRC), 131-133 clinical studies, 94 cloud-based infrastructure tools, 76-77 CoLab, 77 collaboration, 84 commercialization of test assays, 211-234 Defense Production Act (DPA) ratings, 94-95 Deployment Core, 88-93 design review process, 100-101 educational aspects, 84-85 forecasting, 95 GAITS, 77 government entity support, 94 heat map, 97 Independent Test Assessment Program (ITAP), 95-96 initiation of, 17-18 logistical challenges, 93 mission and goal, 74 mitigation strategies, 237 - 248Mobile and At-home Reporting through Standards (MARS), 234 organizational and scheduling support, 97 organizational size, 105–106 outcomes, 85

pandemic response changes, 209-210 process inception, 74-76 professional mindset, 106 quality best practices, 115-116 Regulatory Core, 194-210 roadmap, 75, 89 sample procurement, 96-97 spend-to-date reports, 97 troubleshooting scale-up issues, 95 Variant Task Force (VTF), 93 Rapid Acceleration of Diagnostics (RADx) initiative, building out Clinical Review Committee, 79 Clinical Studies Core, 78 expert network building, 79 Rapid Acceleration of Diagnostics (RADx) initiative, workflow call for proposals, 79 deep dive team, 81-82 Proposal Review Panel, 80 Steering Panel, 82-84 summary, 80 Viability Panel, 80-81 **Regulatory** Core antigen tests, 198-199 **Emergency Use** Authorization, 197-198 FDA and, 196 goals of, 196 molecular tests, 198 origin of, 194-196 testing future, 208 reproduction index (R₀) (sp) defined, 10 early SARS-CoV-2, 10 research and development prioritization vaccine development, 14 World Health Organization (WHO), 12-13 right-of-reference (ROR), 207-208 risk management being mindset, 106 defined, 103 human factors, 107-110 product development process (PDP), 110

risk management

Cambridge University Press & Assessment 978-1-009-39698-1 — Accelerating Diagnostics in a Time of Crisis Steven C. Schachter, Wade E. Bolton Index More Information

Index	2/9

mutation prevalence,

considerations failure modes and effects (FMEA), 121 fault tree analysis (FTA), 121 preliminary hazard analysis (PHA), 121 use-related risk analysis, 121 risk management, regulations and standards 21 CFR 820, 107 ISO 13485, 107 ISO 14971:2019, 107 ISO/TR 24971:2020 Annex H. 107 overview, 107 roadmap comprehensive response, 268 diagnostic test assay laboratory verification, 143 highlight, 264-268 immunology, 32 Mount Sinai Beth Israel (MSBI) medical center clinical management roadmap, 51 pandemic response, 7 quality and risk management, 104 RADx, 75, 89 social impact timeline, 143 **ROSALIND Diagnostic** Monitoring (DxM), 179-182, 239-240 sample pooling media pooling, 138 overview, 138 swab pooling, 138 sample procurement overview, 96-97 SARS-CoV-2. see also COVID-19 pandemic animal testing, 20 disease origin, 19-20 disease progression in China, 11 - 12early reproduction index $(R_0), 10$ horseshoe bats, 20 laboratory analysis methods, 168-171 lineage prevalence, 150 mutation evolution, 168

166-168 quality and risk management roadmap, 104 variant sequencing methods, 171 viral infectivity assessment, 10 viral pathogen sequencing, 10 SARS-CoV-2, immunology adaptive immune response, 39-40 entry into cell, 31-34 herd immunity, 41 infection clinical manifestations, 41-43 innate infection immunity as double-edged sword, 36 - 38innate infection response, 35 - 36overview of normal system, 35 roadmap, 32 serological assays to measure immune response, 43 several components to, 31 vaccination immunity, 43 - 46SARS-CoV-2 Sequencing for Public Health Emergency Response, Epidemiology, and Surveillance (SPHERES) consortium, 172 Sequence Read Archive (SRA), 171 serological assays to measure COVID-19 immune response, 43 shelf-life stability, 204 social impact of COVID-19, direct environmental racism, 252 low socioeconomic position, 250-252 race and ethnic groups, 250 small business closures, 252 women, 253 social impact of COVID-19, indirect health-care access inequalities, 253 public schools, 253

remote learning disparities, 253 socioeconomic position (SEP) and COVID-19, 250-252 South Korea, 14 spend-to-date reports (RADx), 97 stability (Emergency Use Authorization) sample, 201 shelf life, 204 transport, 203-204 Steering Panel (RADx), decision choices WP1, 83-84 WP2, 84 Steering Panel (RADx), member composition, 83 supplier management (QMS), 117-121 supply chain (Deployment Core), 91 surveillance, SARS-CoV-2 genome databases, 171-173 emergence of, 168 global summary table, 169 swab pooling, 138 T-cell responses, 39-40 telemedicine, 56-57 test performance, diagnostic assay sample pooling, 138 trade-offs, 138 toll-like receptor (TLR), 37-38 transport stability, 203-204 21 CFR 820, 106-107, 117 Type I interferon (IFN-1) cellular states due to heterogeneity response, 36 signaling, 36 stochastic layers, 36 United States. see also Rapid Acceleration of Diagnostics (RADx) initiative COVID-19 introduction, 16 - 17lack of national strategic response, 27 Rapid Acceleration of Diagnostics (RADx) initiative, 74-86

usability studies, 206

Cambridge University Press & Assessment 978-1-009-39698-1 — Accelerating Diagnostics in a Time of Crisis Steven C. Schachter, Wade E. Bolton Index More Information

280 Index

use-related risk analysis, 121 vaccination (COVID-19) 2020 NIH public-private partnership, 44 2020 Oxford-AstraZeneca vaccine, 44 Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV), 44 categories, 44 divided social opinion on, 256-257 mitigation strategy, 243 outcome, 44-46 vaccine development early response, 14 Mount Sinai Beth Israel (MSBI) medical center response, 66-68 Variant Task Force (VTF), 93. see also COVID-19 variants biobanking vendor selection, 185 epitope mapping, 185-186 goals of, 178-179 laboratory methods to assess performance, 182-185 organization, 178 policy, 179

ROSALIND Diagnostic Monitoring (DxM), 179 - 182sample banking, 182 Wuhan-Hu-1 wildtype (WT) strain, 182-184 vendors (RADx) procurement, 92-93 troubleshooting issues, 95 viral pathogen sequencing critical for COVID-19 pandemic, 10 SARS-CoV-2 sequence, 10 SARS-CoV-2 Sequencing for Public Health Emergency Response, Epidemiology, an Surveillance (SPHERES) consortium, 172 viral pneumonia label, 9 viral RNA interferon effects, 36 VTF (Variant Task Force) goals of, 150-151 protocol, 152 When To Test (website), 237-238 World Health Organization (WHO) COVID-19 dashboard, 25 - 26COVID-19 pandemic surveillance

recommendations, 22

health emergency declaration, 12 IPPPR error report on response, 26-27 public health and social measures (PHSM), 18 Rapid Acceleration of Diagnostics (RADx) initiative, 17-18 research and development prioritization, 12-13 SARS-CoV-2 sequence, 10 serological assays to measure COVID-19 immune response, 43 variant classification, 176 Wuhan, China travel precautions, 9-10 Wuhan South China Seafood Market first cases, 7 incident management system, 9-10 zoonotic transference, 19 Wuhan-Hu-1 wildtype (WT) variant strain, 182-184 zoonotic monitoring mathematical model, 21 organizations involved

with, 21 zoonotic transference, 19–20