

# Ensuring innovation in diagnostics for bacterial infection

Implications for policy

*Edited by*

**Chantal Morel**

*Research Officer, LSE Health (London School of Economics and Political Science), Faculty of Medicine, University of Geneva*

**Lindsay McClure**

*Research Associate, LSE Health*

**Suzanne Edwards**

*Research Associate, LSE Health*

**Victoria Goodfellow**

*Research Associate, LSE Health*

**Dale Sandberg**

*Research Associate, LSE Health*

**Joseph Thomas**

*Research Assistant, LSE Health*

**Elias Mossialos**

*Professor of Health Policy, LSE Health*

# Table of contents

Acknowledgements	ix
List of abbreviations	xi
List of tables and figures	xv
<b>1. Introduction</b>	<b>1</b>
<b>2. Background</b>	<b>3</b>
2.1 Trends in the use and misuse of antibiotics	3
2.2 Trends in the prevalence of resistance	7
<b>3. Overview of the diagnostics market</b>	<b>13</b>
3.1 Introduction	13
3.2 Shape and size of the market	13
3.3 Recent trends in the market	16
3.4 Exhibits: examples of recent breakthroughs in diagnostic development	25
<b>4. Supply-side bottlenecks inhibiting development of priority diagnostics</b>	<b>33</b>
4.1 Introduction	33
4.2 Drivers of resource allocation decisions by developers and prospective diagnostic developers	33
4.3 Scientific and technical barriers	40
<b>5. Reimbursement-related signals received from procurement and reimbursement agencies</b>	<b>57</b>
5.1 Introduction	57
5.2 Background: reimbursement in the United States	57
5.3 Coverage: determining clinical utility	58
5.4 Background: overview of reimbursement of diagnostics in the United Kingdom and Europe	77
5.5 Implications of being tied to indication	81
5.6 Variation across countries	84
5.7 Reimbursement case study	86

<b>6. Regulation</b>	<b>89</b>
6.1 Introduction	89
6.2 History of medical device regulation	89
6.3 Evolving needs for medical device regulation	90
6.4 Overview of regulatory processes for market entry in Europe and the United States	90
6.5 United States current regulatory structures/frameworks	92
6.6 EU current regulatory structures/framework	102
6.7 Reform under way in the United States	108
6.8 Reforms under way in Europe	115
6.9 Industry stakeholder involvement in European regulatory reforms	118
6.10 Evaluation of communication pathways between regulator and industry	118
6.11 FDA flexibility in antibiotic approval/trial design which may influence uptake of diagnostics	121
6.12 Flexibility in clinical trial requirements for antibiotic development	121
6.13 Regulatory comparison United States/EU	122
6.14 Harmonization of the diagnostics regulatory pathway in the United States and EU	125
6.15 Industry perspectives on harmonization	128
6.16 Stakeholder perception of overall regulatory processes for diagnostics	129
<b>7. Intellectual property challenges</b>	<b>133</b>
7.1 Introduction	133
7.2 History	133
7.3 Patent-related bottlenecks to diagnostic development	136
<b>8. Demand-side issues</b>	<b>145</b>
8.1 Introduction: complexity in demand expression	145
8.2 Engagement to improve developer understanding of demand	146
8.3 Determinants of and barriers to uptake of new POC diagnostics	148
8.4 Diagnostic and clinical guidelines	155
8.5 Prescribing culture	161
8.6 Patient barriers	164
<b>9. Economic evaluation: the limited evidence base affecting both supply and demand for new diagnostics</b>	<b>165</b>
9.1 Introduction	165
9.2 Background: economic evaluation and cost-effectiveness	165
9.3 Background: economic evaluation in the United States	167
9.4 Background: summary of the evidence from economic evaluations of rapid POC diagnostics	170
9.5 Challenges in making the "business case" for new diagnostics	178

9.6	Need for greater role of public sector in setting format priorities	182
9.7	Cost-effectiveness evidence in reimbursement decisions	183
9.8	Technical matters surrounding published cost-effectiveness studies of rapid POC diagnostics	185
<b>10.</b>	<b>Underlying and purpose-driven health system incentives affecting demand for diagnostics</b>	<b>193</b>
10.1	Introduction	193
10.2	Reimbursement	193
10.3	Organization of budgets	200
10.4	Group purchasing	201
10.5	Performance assessment	203
10.6	Public performance monitoring	206
10.7	Financial penalties for poor performance	206
10.8	Financial bonuses for positive performance	207
<b>11.</b>	<b>Co-development of antibiotics and diagnostics for bacterial infection</b>	<b>209</b>
11.1	Introduction	209
11.2	Potential of co-development	209
11.3	Background: the nature and underlying differences in the market for antibiotics and diagnostics	210
11.4	Considerations for co-development strategies	215
<b>12.</b>	<b>Policy response</b>	<b>235</b>
12.1	Rationale for intervention in the diagnostics market	235
12.2	Initiatives to support diagnostics development	236
12.3	Final recommendations	259
<b>Appendix A:</b>	<b>Summary of studies on the cost-effectiveness of POCTs to diagnose sepsis</b>	<b>263</b>
<b>Appendix B:</b>	<b>Summary of studies on the cost-effectiveness of POCTs to diagnose UTI</b>	<b>265</b>
<b>Appendix C:</b>	<b>Streptococcal pharyngitis cost-effectiveness studies</b>	<b>269</b>
<b>Appendix D:</b>	<b>United Kingdom HGC recommendations 2010</b>	<b>273</b>
<b>Appendix E:</b>	<b>Recommendations of the SACGHS to the United States DHHS in 2010 report</b>	<b>275</b>