

Ensuring innovation in diagnostics for bacterial infection

Implications for policy

Edited by
Chantal Morel
Lindsay McClure
Suzanne Edwards
Victoria Goodfellow
Dale Sandberg
Joseph Thomas
Elias Mossialos

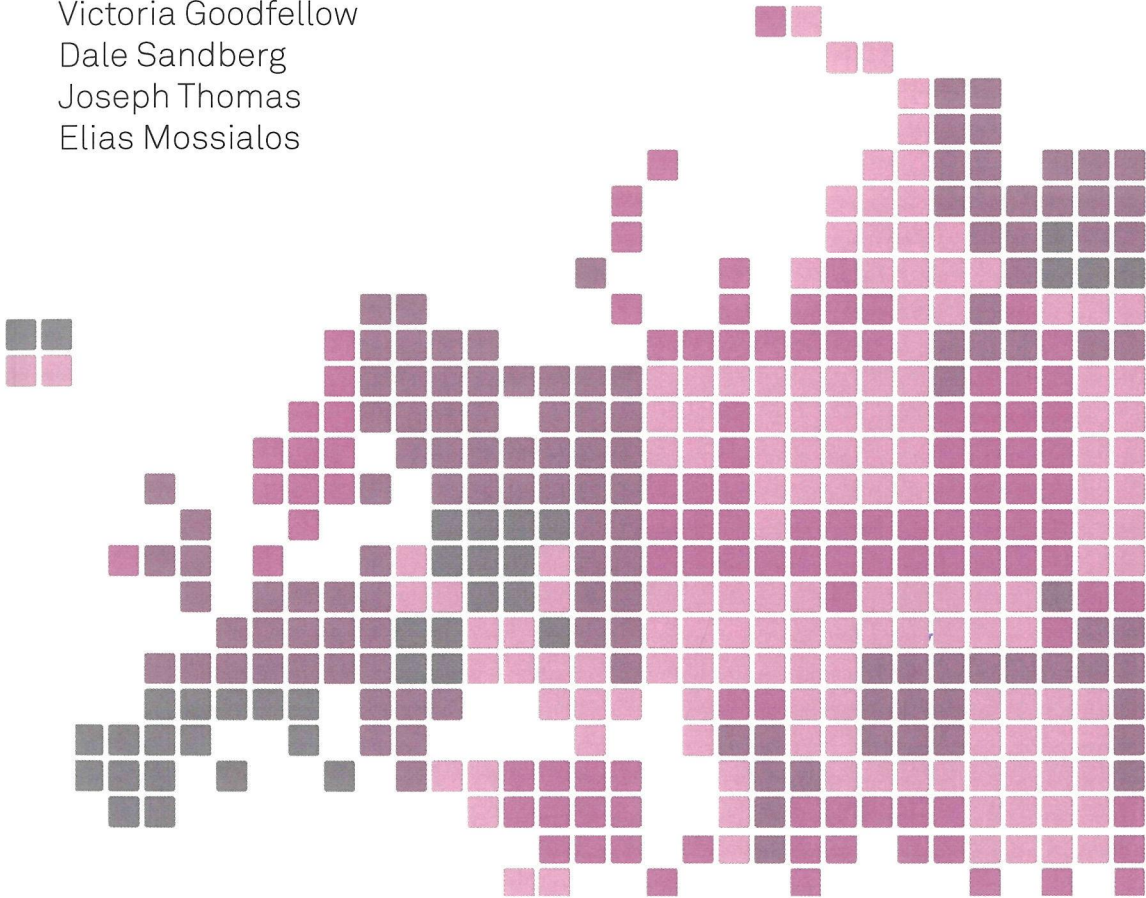


Table of contents

| | |
|--|-----------|
| Acknowledgements | ix |
| List of abbreviations | xi |
| List of tables and figures | xv |
| 1. Introduction | 1 |
| 2. Background | 3 |
| 2.1 Trends in the use and misuse of antibiotics | 3 |
| 2.2 Trends in the prevalence of resistance | 7 |
| 3. Overview of the diagnostics market | 13 |
| 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 |
| 4. Supply-side bottlenecks inhibiting development of priority diagnostics | 33 |
| 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 |
| 5. Reimbursement-related signals received from procurement and reimbursement agencies | 57 |
| 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 |

| | |
|---|------------|
| 6. Regulation | 89 |
| 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 |
| 7. Intellectual property challenges | 133 |
| 7.1 Introduction | 133 |
| 7.2 History | 133 |
| 7.3 Patent-related bottlenecks to diagnostic development | 136 |
| 8. Demand-side issues | 145 |
| 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 |
| 9. Economic evaluation: the limited evidence base affecting both supply and demand for new diagnostics | 165 |
| 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 |
| 10. | Underlying and purpose-driven health system incentives affecting demand for diagnostics | 193 |
| 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 |
| 11. | Co-development of antibiotics and diagnostics for bacterial infection | 209 |
| 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 |
| 12. | Policy response | 235 |
| 12.1 | Rationale for intervention in the diagnostics market | 235 |
| 12.2 | Initiatives to support diagnostics development | 236 |
| 12.3 | Final recommendations | 259 |
| Appendix A: | Summary of studies on the cost-effectiveness of POCTs to diagnose sepsis | 263 |
| Appendix B: | Summary of studies on the cost-effectiveness of POCTs to diagnose UTI | 265 |
| Appendix C: | Streptococcal pharyngitis cost-effectiveness studies | 269 |
| Appendix D: | United Kingdom HGC recommendations 2010 | 273 |
| Appendix E: | Recommendations of the SACGHS to the United States DHHS in 2010 report | 275 |