“Late You Come: Legislation on Lyme Treatment in an Era of Conflicting Guidelines”

Jaan Peter Naktin, MD
Practice Leader, Lehigh Valley Physicians Group - Infectious Diseases, Lehigh Valley Health Network, Allentown, Pennsylvania

Keywords. guidelines; Lyme disease.

In a recent letter [1] to the Ethicist section of the Sunday New York Times Magazine, an anonymous author questioned the actions of a physician as described below:

“… Every patient she sees comes back with a diagnosis of a Lyme-related “condition.” Most of her treatments are not covered by insurance, because they have no basis in evidence, and cost her patients $30 000 a year or more. Moreover, the test she uses for “diagnosis” has never been validated and is not used in New Jersey or New York; all her samples have to be shipped to a lab out of state.”

This is a common scenario seen by many physicians on the front lines of the evaluation and assessment of possible Lyme disease cases, but the response of the ethicist is concerning:

“Good intentions are perfectly consistent with your suspicion that she’s doing harm here, in violation of the Hippocratic Oath. That’s a bad thing, but alas, I’m not sure you can do a lot about it. You could make your case in conversation with those of her patients you’re acquainted with. Given what they already know, though, my bet is that they won’t take much notice. You could also file a complaint with the New Jersey State Board of Medical Examiners, but your identity may not remain confidential if it proceeds against this doctor. And this would be a hard case to bring if, as I fear, most of her patients are grateful for their Lyme-disease diagnosis.”

What is the current environment of care regarding Lyme disease?

HISTORY OF THE MOST RECENT INFECTIOUS DISEASES SOCIETY OF AMERICA GUIDELINES

Updated Lyme disease guidelines are due to be published by the Infectious Diseases Society of America (IDSA) in 2018.

The previous IDSA guidelines for the prevention, diagnosis, and treatment of Lyme disease were published in 2006 [2] and had been the subject of scrutiny, the most notorious being that of the Attorney General Richard Blumenthal of the State of Connecticut who conducted an antitrust investigation into those guidelines, which led to a settlement (agreement) with the IDSA [3]. His findings [4] noted that “The IDSA’s 2006 Lyme disease guideline panel undercut its credibility by allowing individuals with financial interests—in drug companies, Lyme disease diagnostic tests, patents, and consulting arrangements with insurance companies—to exclude divergent medical evidence and opinion.” The antitrust investigation was initiated at the behest of several Lyme disease advocacy groups in existence at the time including the California Lyme Disease Association (CLDA) and the Lyme Disease Association.

Subsequent analysis of these events has appeared in several peer-reviewed journals including the IDSA 2010 “Final Report of the Lyme Disease Review Panel of the IDSA” in Clinical Infectious Diseases [5] with the conclusion that, “After multiple meetings, a public hearing, and extensive review of research and other information, the Review Panel concluded that the recommendations contained in the 2006 guidelines were medically and scientifically justified on the basis of all of the available evidence and that no changes to the guidelines were necessary,” The Centers for Disease Control and Prevention (CDC) continues to endorse the IDSA guidelines as they “continue to provide comprehensive, accurate information that patients can use in their health care decisions” [6].

Johnson and Stricker [7], both of whom have strong affiliations with the CLDA and International Lyme and Associated Disease Society (ILADS), wrote in The Journal of Medical Ethics in 2009, “There are two broad themes that set the stage for the investigation by the Attorney General. The first is the growing problem of conflicts of interest among guidelines developers, and the second is the increasing centralization of medical decisions by insurance companies, who use treatment guidelines as a means of controlling the practices of individual doctors.” The then President of the IDSA, Anne Gershon, had responded in writing to this opinion piece stating that the article was “riddled with inaccuracies and misleading information.” [8] For example, she noted, Among the many inaccuracies in this
The rapid expansion of Tick-Borne Diseases (TBD) in the U.S. and Pennsylvania is further complicated by a lack of consensus among researchers and healthcare practitioners (HCPs) in many critical areas. There are two organizations that have published guidelines for diagnosis and treatment of Lyme and other TBDs: the Infectious Disease Society of America (IDSA), and the International Lyme and Associated Diseases Society (ILADS). The medical community varies in its approach to treating patients with Lyme disease, for example, the adherence to a specific timeframe for antibiotic treatment. Others assess patient response to determine treatment. Pennsylvania’s Task Force members considered both perspectives as well as public health considerations in their deliberations. Representation of the diversity of these views was directed by Act 83, which explicitly called for a “broad spectrum of views to be represented and communicated to patients,” and is reflected in this report and its core recommendations.

The Pennsylvania task force also included a representational blend of government agencies, scientists, providers, and patients with what could be described as a very even mix of those with interest in or experience in Lyme disease. It is not known how much the Connecticut settlement with the IDSA influenced the composition of the panel in Pennsylvania, as it pertains to inclusion of the ILADS members. The recommendations of this task force steered away from anything controversial such as defining the need for long-term antibiotic treatments in patients with persisting symptoms potentially attributable to Lyme disease or the Post-Treatment Lyme Disease Syndrome.

As a follow up to the Act 83 report, the Pennsylvania Legislative Budget and Finance Committee issued a report [14] on October 19, 2016. This report highlights some of the cost challenges faced by the findings of the task force. For example, “No state had dedicated significant resources to fund Lyme disease research, at least in recent years. Many states, however, receive federal funding for various Lyme disease research programs. Pennsylvania has received few such funds ($4.60 per confirmed case).” As to the Education and Awareness issue it was noted that, “To develop and send informational brochures to PA family practice physicians would cost about $772,000. If delivered by persons competent to speak about Lyme disease, costs would be about $2.2 million.” Funds for such initiatives have not been allocated, and a quick addition of the costs estimates would exceed 80 million dollars. Not much else is visibly apparent from the findings of the report except that Pennsylvania has declared Lyme awareness month in May of 2016 in Senate Resolution no. 338 [15] Session of 2015. The language of the resolution states that, “WHEREAS, If not caught early, Lyme disease can lead to chronic debilitating illness that is very difficult to eradicate”, which in and of itself seems to capture and validate the notion that there is a chronic and persistent form of the disease.
Pennsylvania is on the verge of enacting legislation, partially on
2014 as well as absence of the IDSA guidelines from 2006.
ILADS guidelines [17], which have been revised as of September
up to date at the NGC are removed after 5 years.
compliance with current standards” . Guidelines that are not kept
from the NGC in 2015 because they were “outdated and not in
healthcare professionals. The IDSA’s guidelines were removed
courses of antibiotics as an option when deemed necessary by
by the NGC in 2014. These guidelines recommend longer-term
treatments and remove from licensing board scrutiny those that
prescribe long-term antibiotic treatments.
Other states including California, Connecticut, Massachusetts,
Minnesota, New Hampshire, New Jersey, and New York have
enacted similar legislation that either mandates insurance pay-
ment for long-term antibiotics or protects doctors who prescribe
long-term treatment (see Appendix B of the Lyme Disease in
Pennsylvania report) [13].
Federal Legislation has been introduced, “H.R.789 - Tick-
Borne Disease Research Accountability and Transparency Act
of 2015 [18]”, and is a step in the direction of national Lyme
legislation and had made provisions for the establishment of an
“Interagency Lyme and Tick-Borne Disease Working Group.”
Composition of this committee is not specific, but it is proposed
to include “Physicians and other medical providers with experi-
ence in diagnosing and treating Lyme disease and other tick-
borne diseases” and “in making appointments … the Secretary,
the Speaker of the House of Representatives, and the Majority
Leader of the Senate shall ensure that the non-Federal public
members of the Working Group represent a diversity of scient-
ific perspectives.” The language is remarkably similar to the
language used in PA Act 83 of 2014. It is not known at this time
who has been selected for this panel, although the committee is
to include “patients and their family members” and “nonprofit
organizations that advocate for patients with respect to tick-
borne diseases”, which can only mean ILADS, the Lyme Disease
Association, or an affiliated entity.

INTERNATIONAL LYME AND ASSOCIATED DISEASE
SOCIETY
What is the role of an organization such as ILADS, which has
no affiliation with the IDSA, in guideline development and/or
legislative efforts? They describe their mission statement [19]
as follows:
“ILADS is a nonprofit, international, multidisciplinary
medical society dedicated to the appropriate diagnosis and
treatment of Lyme and associated diseases. ILADS promotes
understanding of Lyme and associated diseases through
research, education and policy. We strongly support physi-
cians, scientists, researchers and other healthcare profes-
sionals dedicated to advancing the standard of care for Lyme and
associated diseases.”
As such, ILADS maintains its own set of competing Lyme dis-
ease guidelines [20]: “Evidence assessments and guideline
recommendations in Lyme disease: the clinical management
of known tick bites, erythema migrans rashes and persistent
disease.” These guidelines are also housed [17] at the NGC.
Incidentally, review of NGC guidelines indicates that the “The
NGC does not develop, produce, approve, or endorse the guide-
lines represented on this site. All guidelines summarized by
NGC and hosted on our site are produced under the auspices of
medical specialty societies, relevant professional associa-
tions, public or private organizations, other government agen-
cies, health care organizations or plans, and similar entities.”
Being an entity associated with the Department of Health and
Human Services and the Agency for Healthcare Research and
Quality (AHRQ), and intending to abide by the 2011 Institute
of Medicine (IOM) Report on Trustworthy Guidelines, it is noted
on the NGC website that “The NGC is finalizing the AHRQ-
approved process of assessing Clinical Practice Guidelines
(CPG) against select standards/sub-standards. Following this,
NGC will begin assessing guidelines in our work queue and will
then add assessment results to the Web display. We anticipate
that the process of determining and posting the extent adher-
ence of guidelines against the IOM standards may begin by the
summer of 2017.” [21] It is not clear how this may impact exist-
ing guidelines such as those promoted by ILADS.
Review of the ILADS-submitted guidelines shows that 12
of the 12 recommendations are done so with the lowest of all
the ratings, ie, “very low quality evidence”, with the caveat that
“a strong recommendation may be made in the face of very
low-quality evidence when the risk–benefit analysis favors a
particular intervention such that most patients would make
the same choice.” The preamble to the ILADS guidelines also
suggests that the overall system of guideline development is
flawed, and their approach to the prevention and treatment of
Lyme disease is based on necessity and not sound scientific evi-
dence. “When the evidence base is of low or very low quality,
guideline panels should be circumspect about making strong
recommendations to avoid encouraging uniform practices that are not in the patient’s best interest and to ensure that research regarding benefits and risks is not suppressed” [22, 23] There is no current national systematic approach for achieving consensus on conflicting guidelines [24].

The ILADS is registered as a 503(c)6 nonprofit organization with public reporting of their 990 tax forms, but associated organizations and practices are owned privately. The ILADS, despite their existing guidelines and significant presence at sentinel legislative occurrences, has not been included in the list of participants in the upcoming revised IDSA guidelines [25]. Review of the IDSA Handbook on Clinical Practice Guideline Development [26] and the Project Plan [27] for the upcoming Lyme diseases guidelines confirms that ILADS or other associated entities has not had any representation in the development of the new guidelines.

In Pennsylvania, there is a sophisticated website [28], “PA Lyme Resource Network”, that is apparently run as a nonprofit charitable organization by one of the members of the PA Task Force on Lyme Disease with the stated goal to “help others navigate this exceedingly complex and controversial disease.” The website maintains links to ILADS, and their referral network and laboratory services are known for their “home brew” laboratory developed tests [29]. Their “advocacy” does not include any links to the CDC, IDSA, or other Infectious Diseases experts in Pennsylvania.

There is no reporting by ILADS or its affiliated entities regarding the numbers of patients diagnosed and treated. Their fee schedules are also not displayed nor are any potential conflicts of interest with partnership or ownership in affiliated laboratory entities. Data such as treatment regimens, numbers and types of antibiotics used, supplements prescribed, side effects, and adverse outcomes are also impossible to ascertain. Most entities seem to be fee-for-service and do not accept insurances, are not directly associated with any parent academic institution or healthcare organization, and do not maintain electronic records, or at least are not part of shared records across systems. All of these observations are made also with the understanding that all of their recommendations are made with “very low quality evidence.”

The 2011 Lancet Infectious Diseases article “Anti-science and Ethical Concerns Associated with Advocacy of Lyme Disease” [30] does an excellent review of the events described herein, noting that “activists, through public appeal and political lobbying, have managed to divert attention away from existing evidence-based medicine in their quest to redefine Lyme disease. There is a serious concern that they will further endanger the public’s health unless responsible physicians, scientists, government leaders, and the media firmly stand up for an evidence-based approach to this infection that is based on high-quality scientific studies.” This article was published 6 years ago, and the situation has only deteriorated, with inclusion of the same influences at high levels of government decision-making as evidenced by recent events and legislative efforts in Pennsylvania.

It is very possible that the unintended consequences of these legislative activities will be public acceptance of medicine that is not evidence based, which in turn leads to more antibiotics being prescribed for conditions that may not be related to Lyme disease. Additional antibiotic courses then cause resistant strains of bacteria to emerge, disruption of the microbiome, emergence of Clostridium difficile, and delay in diagnosis of other serious medical conditions. Many of these issues were articulated by Leonard Sigal in 1996: “Lyme disease represents a complex epidemiological, clinical, and health care planning problem. Patients and the lay public are increasingly frustrated with their perception that the medical community is not listening to them and is ignoring the real problems that are the roots of their anxieties: the slow pace of research, inattention to aspects of LD they find most important, disbelief of their symptoms and severity of their illness, and physicians’ detachment and lack of sympathy and sensitivity” [31]. Unfortunately, the situation has not improved since then, and it is perhaps getting worse, as evidenced by a recent Morbidity and Mortality Weekly Report that highlighted “Serious Bacterial Infections Acquired During Treatment of Patients Given a Diagnosis of Chronic Lyme Disease” [32].

CONCLUSIONS

What may have been seen in the past as a fundamentally patient-driven movement has achieved a scale and proportion, with the involvement of legitimate legislative state authority—at least in Pennsylvania—and the growth of organizations such as ILADS and affiliated entities, that is indeed a rival to the position and power held by the IDSA and “conventional medicine” in the past.

As per the Friedrich Schiller quotation, “Spät kommt ihr doch ihr kommt!”, which is translated as “You come late, yet you come!,” and so may be the fate of the upcoming 2018 updated and revised Lyme disease guidelines. There is no deus ex machina, as it may pertain to the impending scientific salvation of Lyme disease diagnosis and treatment, because it may already be a lost cause due to the current environment in which potential cases of Lyme disease here in Pennsylvania, and nationally, are evaluated and treated. It is not enough to rely on guidelines, or the application or revision of guidelines, in this environment to make care better.

There are 2 strong measures that could be used to improve this situation. (1) In the era of the Accountable Care Organization (ACO) and population health, the resources of large and significant healthcare entities could be used to promote prevention, diagnosis, and treatment of Lyme disease in a more organized, systematic, and reproducible way with ties to public reporting and accountability. Payment systems for the ACOs are already linked to quality, outcomes, and shared risk [33]. (2) By the same token, entities, such as ILADS, who promote nonevidence-based medicine, should be held equally accountable for their diagnoses and treatment plans with some aspect of public reporting in financial interests, relationships with testing entities, numbers of patients treated, treatment regimens, and outcomes.
Johnston and Stricker [7] had previously written that, "At a minimum, the guidelines issued by a dominant medical society should conform to fundamental rules of due process, fairness, and accuracy." Transparency should also be applicable to the practice patterns of any entity, dominant or not, that puts itself forward as promoting "understanding of Lyme and associated diseases through research, education, and policy," especially as the foundations of statewide or national legislation are laid.

Throughout its history, Lyme disease has been a slow burning public health crisis. There can no longer be 2 systems of diagnosis and treatment; it is time that all levels of care are held equally accountable and transparent at a statewide and national level.

Acknowledgments

Potential conflicts of interest. The author: No reported conflicts of interest. All authors have submitted the ICJME Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Appiah KA. What To Do About A Physician Who May Be A Quack. Available at: https://www.nytimes.com/2017/01/11/magazine/what-to-do-about-a-physician-who-may-be-a-quack.html Accessed 20 April 2017.
2. Wormser GP, Dattwyler RJ, Shapiro ED, et al. The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: Clinical Practice Guidelines by the Infectious Diseases Society of America. Clin Infect Dis 2006; 43:1089–134.
3. Connecticut Office of the Attorney General and the Infectious Diseases Society of America. An Agreement Between the Attorney General of the State of Connecticut and the Infectious Diseases 2008. Available at: http://www.ct.gov/ag/lib/ag/health/idsaagreement.pdf. Accessed 20 April 2017.
4. Blumenthal R. Statement to the Press 2008. Available at: http://www.ct.gov/ag/cwp/view.asp?a=27958q=414284. Accessed 20 April 2017.
5. Lantos PM, Charini WA, Medoff G, et al. Final report of the Lyme disease review panel of the Infectious Diseases Society of America. Clin Infect Dis 2010; 51:1–5.
6. Centers for Disease Control and Prevention. Lyme Disease Frequently Asked Questions. Available at: https://www.cdc.gov/lyme/faq/index.html. Accessed 20 April 2017.
7. Johnson L, Stricker RB. Attorney General forces Infectious Diseases Society of America to redo Lyme guidelines due to flawed development process. J Med Ethics 2009; 35:283–8.
8. Gerishon A. Lyme Article Was Riddled with Inaccuracies—Putting Patients at Risk. J Med Ethics 2009. Available at: http://jme.bmj.com/content/35/5/283.
9. Johnson L, Stricker RB. The Infectious Diseases Society of America Lyme guidelines: a cautionary tale about the development of clinical practice guidelines. Philosophy, Ethics, and Humanities in Medicine. 2010; 5:9 Available at: http://www.peh-med.com/content/5/1/9. Accessed 20 April 2017.
10. Lantos PM, Charini WA, Medoff G, et al. Final report of the Lyme disease review panel of the Infectious Diseases Society of America. Clin Infect Dis 2010; 51:1–5.
11. Centers for Disease Control and Prevention. Reported cases of Lyme disease by state or locality. 2006-2016 Available at: https://www.cdc.gov/lyme/stats/tables.html. Accessed 20 April 2017.
12. Adron ER, Aucott J, Lemke KW, Weiner JP. Health Care Costs, Utilization and Patterns of Care following Lyme Disease. PLoS One 2015; 10(e116767).
13. Aguilar TJ, et al. LYME DISEASE IN PENNSYLVANIA: A Report Issued by the Task Force on Lyme Disease and Related Tick-Borne Diseases Pursuant to Act 83 of 2014 (September 2015). Available at: http://www.health.pa.gov/Md%20Health/Diseases%20And%20Conditions/I/Document/Lyme%20Disease%20In%20Pennsylvania%20(2).pdf. Accessed 20 April 2017.
14. Legislative Budget and Finance Committee, State of Pennsylvania. Report Highlights: Cost Estimates to Implement the Recommendations of the Task Force on Lyme Disease and Related Tick-borne Diseases 2016. Available at: http://bitc legis.state.pa.us/Resources/Documents/Reports-Highlights/571.pdf. Accessed 20 April 2017.
15. The General Assembly of Pennsylvania. Greenleaf, et al. SENATE RESOLUTION No. 338. Designating the month of May 2016 as "Lyme Disease Awareness Month" in Pennsylvania 2016. Available at: http://www.legis.state.pa.us/cfdocs/legis/ PN/Public/btCheck.cfm?txtType=PDF&sessYear=2015&sessInd=0&billBody=S&billTyp=R&billNbr=0338&pn=1697. Accessed 20 April 2017.
16. The General Assembly of Pennsylvania: Greenleaf, et. al An Act providing for patient access to diagnostics and treatments for Lyme disease and related tick-borne illnesses; and requiring health care policies to provide certain coverage 2016. Available at: http://openstates.org/pa/bills/2015–2016/SB1299/. Accessed 20 April 2017.
17. National Guideline Clearinghouse (NGC). Guideline summary: Evidence assessments and guideline recommendations in Lyme disease: the clinical management of known tick bites, erythema migrans rashes and persistent disease. In: National Guideline Clearinghouse (NGC) [Web site]. Rockville (MD): Agency for Healthcare Research and Quality (AHRQ); 2014. Available at: https://www.guideline.gov/summaries/summary/49320/evidence-assessments-and-guideline-recommendations-in-lyme-disease-the-clinical-management-of-known-tick-bites-erythema-migrans-rashes-and-persistent-disease.cq-lyme. Accessed 20 April 2017.
18. Rep. Gibson, Christopher P.H.R.789. Tick-Borne Disease Research Accountability and Transparency Act of 2015114th Congress (2015–2016). Available at: https://www.congress.gov/bill/114th-congress/house-bill/789/text. Accessed 20 April 2017.
19. ILADS. The International Lyme and Associated Disease Society (ILADS) Mission Statement. Available at: http://www.ilads.org/ilads/mission-statement.php. Accessed 20 April 2017.
20. The International Lyme and Associated Disease Society (ILADS). Treatment Guidelines Evidence Assessments and Guideline Recommendations in Lyme disease: the Clinical Management of Known Tick Bites, Erythema Migrans Rashes and Persistent Disease. Available at: http://www.ilads.org/lyme/treatment-guideline-lymephp. Accessed 20 April 2017.
21. The National Guideline Clearinghouse. The National Guideline Clearinghouse Extent Adherence to Trustworthy Standards (NEATS) Assessments. Available at: https://www.guideline.gov/help-and-about/summaries/determining-extent-adherence-to-the-iom-standards-in-ngc. Accessed 20 April 2017.
22. Scott IA, Guaytt GH. Suggestions for improving guideline utility and trustworthiness. Evid Based Med 2014; 19:91–6.
23. Cameron, Daniel I, Johnson LB, Maloney EL. Evidence assessments and guideline recommendations in Lyme disease: the clinical management of known tick bites, erythema migrans rashes and persistent disease. Expert Rev Anti Infect Ther 2014; 12: 1103–1135. Available at: http://www.tandfonline.com/doi/full/10.1586/14787210.2014.940900. Accessed 20 April 2017.
24. Institute of Medicine. Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press; 2011.
25. Wormser GP, Dattwyler RJ, Shapiro ED, et al. The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: Clinical Practice Guidelines by the Infectious Diseases Society of America. Clin Infect Dis 2006; 43:1089–134.
26. Infectious Diseases Society of America. Handbook on Clinical Practice Guideline Development, Infectious Diseases Society of America (IDSA), v. 10.2015. Available at: https://www.idsociety.org/UploadedFiles/IDSA/Guidelines_Patient_Care/Guidelines_By_Others/IDSA%20Handbook%20on%20CPG%20Development%2010.15.pdf. Accessed April 2017.
27. Infectious Diseases Society of America. Project Plan: Guidelines for the Prevention, Diagnosis, and Treatment of Lyme Disease by the Infectious Diseases Society of America, the American Academy of Neurology, and the American College of Rheumatology, March 2015. Available at: http://www.idsociety.org/uploadedFiles/IDSA_Topics_of_Interest/Lyme_Disease/Project%20Plan%20March%202015.pdf. Accessed 20 April 2017.
28. PA Lyme Resource Network. PA Lyme Resource Network: Pennsylvania’s Resource for Lyme prevention, education, patient support and advocacy. Available at: http://paylyme.org/. Accessed 20 April 2017.
29. Aguerro-Rosenfeld ME, Wormser GP. Lyme disease: diagnostic issues and controversies. Expert Rev Med Diagn 2015; 15:1–4.
30. Auwaerter PG, Bakken JS, Dattwyler RJ, et al. Anti-science and ethical concerns Given a Diagnosis of Chronic Lyme Disease—United States.” MMWR. Morbidity and Mortality Weekly Report 2016; 65. Available at: https://www.cdc.gov/mmwr/vol-65/rr-16.pdf. Accessed 20 April 2017.
31. Sigal LH. “The Lyme disease controversy: social and financial costs of misdiagnosis and mismanagement.” Arch Intern Med 1996; 156:1493–500.
32. Marzec NS. “Serious Bacterial Infections Acquired During Treatment of Patients Given a Diagnosis of Chronic Lyme Disease—United States.” MMWR. Morbidity and Mortality Weekly Report 2017; 66. Available at: https://www.cdc.gov/mmwr/vol-66/wr/mm6603a3.htm. Accessed 16 June 2017.
33. Department of Health and Human Services Centers for Medicare and Medicaid Services. Accountable Care Organizations: What Providers Need to Know, March 2016. Available at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/sharedsavingsprogram/Downloads/ACO_Providers_Factsheet_ICN907406.pdf. Accessed 13 June 2017.

PERSPECTIVES • OFID • 5