

### **PROJECT MUSE**\*

Swann Song: Antibiotic Regulation in British Livestock Production (1953–2006)

Claas Kirchhelle

Bulletin of the History of Medicine, Volume 92, Number 2, Summer 2018, pp. 317-350 (Article)

Published by Johns Hopkins University Press *DOI:* https://doi.org/10.1353/bhm.2018.0029



➡ For additional information about this article https://muse.jhu.edu/article/698175



#### Swann Song: Antibiotic Regulation in British Livestock Production (1953–2006)

CLAAS KIRCHHELLE

SUMMARY: Antibiotics have played a significant yet ambivalent role in Western livestock husbandry. Mass introduced to agriculture to boost animal production and reduce feed consumption in the early 1950s, agricultural antibiotics were soon accused of selecting for bacterial resistance, causing residues and enabling bad animal welfare. The dilemma posed by agricultural antibiotic regulation persists to this day. This essay traces the history of British antibiotic regulation from 1953 to the influential 1969 Swann report. It highlights the role that individual experts using bacteriophage typing played in warning about the mass selection for bacterial resistance on farms and the response of a corporatist system, whose traditional laissez-faire arrangements struggled to cope with the risk posed by bacterial resistance. In addition to contextualizing the Swann report's origins, the essay also discusses the report's fate and implications for current antibiotic regulation.

KEYWORDS: agricultural antibiotics, antimicrobial resistance, Swann report, drug regulation, precautionary regulation

Agricultural antibiotics have played a significant role in global food production for over sixty years. Antibiotic use on farms confers three advantages: antibiotics combat pathogens; their prophylactic use can prevent the spread of infection; and, if given regularly, even low doses of antibiotics promote animals' growth and reduce feed intake. However, agricultural

Numerous people have contributed to this article. I am especially grateful to Mark Harrison, Christoph Gradmann, Scott Podolsky, and Ulrike Thoms for reading and commenting on article drafts. I would also like to thank participants of the 2013 DRUGS network "Futures Past and Present: Hopes and Fears and the History of Antibiotic Resistance" workshop for their helpful comments on the first draft of this article. I equally owe a large debt of gratitude to the anonymous reviewers of this essay for their very helpful comments and suggestions. My research was originally funded by a Wellcome Trust doctoral fellowship and later by the Oxford Martin School. I would like to thank the British National Archives and the Wellcome Collection for granting access to their archival material.

317 Bull. Hist. Med., 2018, 92: 317-351

antibiotic use has an equal number of disadvantages: it can cover up bad animal husbandry, and residues in food and the environment can create or trigger antibiotic allergies.<sup>1</sup> Most importantly, every use of antibiotics can select for bacterial resistance. While agricultural antibiotics' overall contribution remains contested, resistant bacterial infections now pose one of the greatest threats to global health.<sup>2</sup>

In this situation, it is important to understand the historical trajectories and decisions shaping antibiotic consumption. In the case of medical antibiotic use, historians like Christian McMillen and Scott Podolsky have highlighted long-term patterns and constraints underlying public health thinking and regulation.<sup>3</sup> The goal of this essay is to do the same for European agricultural antibiotic regulation, the roots of which lie in 1969. In that year, a report by Britain's Swann committee pioneered a new way of resistance-focused regulation by recommending the precautionary restriction of some widely used antibiotic feeds. However, the report's long-term impact was ambivalent. Despite shaping European antibiotic policy until the 2000s, the report failed to reduce overall antibiotic consumption and bacterial resistance.

This essay reconstructs the genesis of the influential Swann report. It shows that many of the report's precautionary recommendations originated around 1960 and were dominated by scenarios of vertical resistance proliferation. When new research on horizontal gene transfer emerged during the mid-1960s, corporatist power struggles prevented a modification of regulations to account for so-called infectious resistance (resistance proliferation via horizontal gene transfer).

Contrary to popular myths, the essay also shows that antibiotics' mass introduction to agriculture was not solely due to farmers' demands but resulted from officials' belief that antibiotics would reduce feed imports and boost meat production. Between 1953 and 1969, agricultural antibiotics contributed to a substantial growth of veterinary drug sales and the

1. Tony Lawrence, Vernon Fowler, and Jan Novakofski, *Growth of Farm Animals*, 3rd ed. (Wallingford: CABI, 2012), 325–27.

2. Putting Meat on the Table: Industrial Farm Animal Production in America (Washington, DC: PEW Commission on Industrial Farm Animal Production, 2008); Tackling Drug-Resistant Infections Globally: Final Report and Recommendations (London: Review on Antimicrobial Resistance, 2016).

3. Christian McMillen, *Discovering Tuberculosis: A Global History 1900 to the Present* (New Haven, Conn.: Yale University Press, 2015); Scott Podolsky, *The Antibiotic Era: Reform, Resistance and the Pursuit of a Rational Therapeutics* (Baltimore: Johns Hopkins University Press, 2015).

gradual intensification of British livestock husbandry.<sup>4</sup> By the late 1950s, new knowledge about bacterial resistance challenged rising antibiotic use. Employing a technology called phage-typing, researchers affiliated with Britain's Public Health Laboratory Service (PHLS) warned that resistance selection on farms could also harm humans. PHLS data forced officials to establish new boundary values for agricultural antibiotic use. According to Nathalie Jas, Soraya Boudia, and Carsten Reinhardt, boundary values legitimize the continued use of risky technologies and substances and are a compromise between demands for absolute safety and economic interests.<sup>5</sup>

However, deciding which forms of antibiotic use were appropriate and who should control antibiotic access was not easy. At stake was not only control over the lucrative nonhuman drug market but also the relative standing of different professions within Britain's corporatist policy system. Corporatism is traditionally defined as a system in which representative groups assume some responsibility for the self-regulation of their own constituency in return for privileges and a close relationship with government.<sup>6</sup> In Britain, corporatist decision making was particularly pronounced in the health and agricultural sectors. However, antibiotic regulation blurred traditional boundaries. During the 1960s, pharmaceutical firms, farmers-represented by the powerful National Farmers' Union (NFU)-and agricultural experts used corporatist ties to the Ministry of Agriculture, Fisheries, and Food (MAFF) to press for unrestricted antibiotic access in return for voluntary self-regulation. This was not in the interest of British veterinarians. As Abigail Woods, Ulrike Thoms, and Nicolas Fortané have shown, the 1960s witnessed the transition of traditional European veterinary work to mass animal health management.<sup>7</sup> For veterinarians, asserting control over antibiotics was important not only to

4. T. A. B. Corley and Andrew Godley, "The Veterinary Medicine Industry in Britain in the Twentieth Century," *Econ. Hist. Rev.* 64, no. 3 (2011): 832–54, quotation on 832.

5. Soraya Boudia and Nathalie Jas, eds., *Powerless Science? Science and Politics in a Toxic World* (New York: Berghahn, 2014); Carsten Reinhardt, "Boundary Values," in *Precarious Matters /Prekäre Stoffe*, ed. Viola Balz et al. (Berlin: MPI for the History of Science, 2008), 39–50.

6. Graham Cox, Philip Lowe, and Michael Winter, "From State Direction to Self-Regulation: The Historical Development of Corporatism in British Agriculture," *Policy Polit.* 14, no. 4 (1986): 475–90, 475–76.

7. Abigail Woods, "Is Prevention Better Than Cure? The Rise and Fall of Veterinary Preventive Medicine, c. 1950–1980," *Soc. Hist. Med.* 26 (2012): 113–31, esp. 113; Ulrike Thoms, "Handlanger der Industrie oder berufener Schützer des Tieres? Der Tierarzt und seine Rolle in der Geflügelproduktion," in *Was der Mensch essen darf: Ökonomischer Zwang, ökologisches Gewissen und globale Konflikte*, ed. G. Hirschfelder et al. (Wiesbaden: Springer, 2015), 173–92. generate income but to secure their profession's primacy over competing nutritional and health experts.<sup>8</sup> While veterinary and agricultural interests clashed within MAFF, public health experts pressed the Ministry of Health (MH) to restrict both freely available antibiotic growth promoter feeds (AGPs) and veterinary antibiotic prophylaxis. What resulted were nine years of sustained conflict about professional and ministerial powers and the true significance of resistance selection on farms.

Remarkably, these conflicts rarely spilled into the public sphere. As Georg Krücken argues, the credibility of Britain's corporatist system depended on the generation of compromise behind closed doors and the subsequent endorsement of this compromise by all parties.<sup>9</sup> In the case of agricultural antibiotics, confidential negotiations enabled considerable regulatory flexibility but also limited the effectiveness of reforms. This is illustrated by the 1969 Swann report's differentiation between medically relevant and irrelevant antibiotics. The report's partial ban of therapeutic AGPs seemingly reconciled conflicting demands for antibiotic restrictions with agricultural demands for antibiotic access.

However, in aiming for a traditional political compromise, the Swann report failed to address underlying patterns of antibiotic demand and new scenarios of horizontal resistance transfer. By the mid-1970s, it became clear that animal husbandry remained antibiotic dependent and that allegedly nontherapeutic antibiotics could select for resistance against therapeutic antibiotics. Unfortunately, the report's corporatist origins made it difficult for involved parties to criticize the original compromise. Meanwhile, British officials embarked on a successful international campaign of spreading the self-proclaimed Swann gospel. What had arisen as a narrow corporatist compromise geared to solving domestic tensions soon turned into an international policy matrix for antibiotic regulation. In the absence of a critical reevaluation of its origins and blind spots, Swannbased regulations still form a cornerstone of European antibiotic policy.

### From Rationing to Gluttony—The Rise of Agricultural Antibiotics

With the notable exceptions of wartime chemotherapy to treat mastitis in British dairy herds and the veterinary treatment of individual animals, the

<sup>8.</sup> Nicolas Fortané, "Foundation of the Swine Pathology Station in Ploufragan: Transformations in Veterinary Expertise and New Ways of Managing Animal Health in Intensive Livestock Production" (unpublished manuscript, 2015).

<sup>9.</sup> Georg Krücken, Risikotransformation: Die politische Regulierung technisch-ökologischer Gefahren in der Risikogesellschaft (Wiesbaden: Westdeutscher Verlag, 1997).

routine use of sulphonamides and antibiotics was relatively slow to spread in British postwar agriculture.<sup>10</sup> After 1945, a combination of bad harvests and the sudden termination of the American lend-lease agreement left Britain chronically short of food and foreign currency. Prolonged by the Korean War, British rationing and the limitations imposed on animal production ended only in late 1953. By this time, international food prices were falling. However, instead of reverting to prewar doctrines of laissez-faire agriculture, postwar governments promoted a new corporatist policy based on close cooperation with the NFU and cemented by the 1947 Agricultural Act.<sup>11</sup> According to John Martin, the 1947 act had two interrelated aims: "the promotion of a 'stable' agricultural sector to ensure fairer returns for farmers . . . ; and an 'efficient system to increase food production."12 A specific aim of the British government was to expand animal production to satisfy consumers' craving for meat and reduce costly imports. Over the next two decades, a system of price supports encouraged the adoption of new husbandry methods and maximized production.<sup>13</sup>

In pushing for modern animal production methods, British agricultural planners were strongly influenced by postwar developments in U.S. animal production. Mark Finlay and Roger Horowitz have described how U.S. farmers used innovations in nutrition, housing, and breeding to concentrate unprecedented numbers of pigs and poultry in indoor production systems. Because of increased herd densities, many of the intensive production systems came to rely on the routine use of antibiotics to control disease.<sup>14</sup> With arsenicals and sulphonamides already proving popular on U.S. farms,<sup>15</sup> Merck introduced sulfaquinoxaline, the first medicine permitted by the U.S. government to be routinely mixed in animal food in

10. Abigail Woods, "Science, Disease and Dairy Production in Britain,' *Agric. Hist. Rev.* 62, no. 2 (2007): 294–314, 301–2.

11. Michael Winter, Rural Politics: Policies for Agriculture, Forestry and the Environment (London: Routledge, 1996), 101–5; John Martin, The Development of Modern Agriculture: British Farming since 1931 (London: Macmillan, 2000), 75–85.

12. Martin, Development of Modern Agriculture (n. 11).

13. Ibid.

14. Mark Finlay, "Hogs, Antibiotics, and the Industrial Environments of Postwar Agriculture," 237–60, and Roger Horowitz, "Making the Chicken of Tomorrow: Reworking Poultry as Commodities and as Creatures, 1945–1990," 215–35, both in *Industrializing Organisms: Introducing Evolutionary History*, ed. Philip Scranton and Susan Schrepfer (London: Routledge, 2004).

15. Susan Jones, Valuing Animals: Veterinarians and Their Patients in Modern America (Baltimore: Johns Hopkins University Press, 2004), 96–106. 1948 for the treatment of coccidiosis in poultry.<sup>16</sup> One year later, Thomas Jukes and E. L. Stockstad of American Cyanamid's Lederle Laboratories found that the regular consumption of low-concentrated (subtherapeutic) antibiotics in industrial fermentation wastes allowed animals to process their feeds more efficiently and grow faster. AGPs also promised to control bacterial herd infections.<sup>17</sup>

In Britain, the lifting of import restrictions on feedstuffs and the end of rationing in 1953 enabled a growing number of farmers to focus on animal husbandry.<sup>18</sup> The same year Britain legalized the large-scale introduction of antibiotics to agriculture. Prior to 1953, antibiotic access had been restricted by the 1947 Penicillin Act. Fearing bacterial resistance, the government had entrusted antibiotics to physicians and veterinarians by making them prescription-only medicines. It seems remarkable that only six years later, the 1953 Therapeutic Substances (Prevention of Misuse) Act (TSA) allowed the low-dose inclusion of penicillin and chlortetracycline (Aureomycin) into animal feeds.

Government documents reveal that the decision to deregulate antibiotics was not easy: following the U.S. licensing of prescription-free AGPs in 1951,<sup>19</sup> Britain's Agricultural Research Council (ARC) had conducted a series of disappointing feed experiments with domestic penicillin and streptomycin in nonintensive settings.<sup>20</sup> In Whitehall, some officials also expressed concern about the patchy state of scientific knowledge: "The difficulty seems to be that no one apparently knows what the antibiotics does [*sic*] and how it acts."<sup>21</sup> In July 1953, Conservative Minister of Agriculture Tom Dugdale confided to NFU president Sir James Turner that he considered AGP legalization a medical experiment.<sup>22</sup> A particularly contentious decision was allowing farmers to purchase both supplemented feeds and

16. John E. Lesch, *The First Miracle Drugs: How the Sulfa Drugs Transformed Medicine* (Oxford: Oxford University Press, 2007), 287; William Campbell, "History of the Discovery of Sulfaquinoxaline as a Coccidostat," *J. Parasitology* 94, no. 4 (2008): 934–45.

17. Thomas H. Jukes, Antibiotics in Nutrition (New York: Medical Encyclopedia, 1955).

18. Martin, Development of Modern Agriculture (n. 11), 75-85.

19. Claas Kirchhelle, "Pyrrhic Progress: Antibiotics and Western Food Production (1949–2013)" (PhD diss., University of Oxford, 2015), 46.

20. The National Archives of the UK (henceforth TNA) FD 9/1458 (Clements to A. A. Miles, March 28, 1960), 1; Delphine Berdah, "One Health, Two Medicines? Vaccines and Antibiotics in Randomized Control Trials for Humans and Farm Animals in the UK before and after the NHS" (unpublished); R. Braude and K. G. Mitchell, "Antibiotics and Liver Extract for Suckling Pigs," *Brit. J. Nutr.* 6, no. 1 (1952): 398–400, quotation on 398.

21. TNA MAF 119/23 (Minute Hill to Croxford, April 19, 1952).

22. TNA MAF 287/299 (Dugdale to Turner, July 29, 1953), 2.

diluted antibiotic substrates for home-mixing.<sup>23</sup> MH officials warned: "The whole purpose of the Penicillin Act was to prevent . . . antibiotics being used indiscriminately with a consequent danger of producing penicillin resistant strains of pathogens."<sup>24</sup>

However, such opposition proved ineffective. During ministerial meetings, experts claimed that any "risk to health was negligible."<sup>25</sup> Referencing reports on American AGP use, proponents stressed the "immediate increase in agricultural production" and the "saving in . . . feeding stuffs."<sup>26</sup> According to animal nutritionist Raphael Braude of the National Institute for Research in Dairying, veterinarians and physicians could resort to other antibiotics in the case of penicillin resistance.<sup>27</sup> The British Veterinary Association (BVA) and the Royal College of Veterinary Surgeons (RCVS) did not oppose AGPs either.<sup>28</sup>

Unsurprisingly, antibiotic manufacturers also promoted AGPs' licensing: following the failure of domestic feed trials, the British government approached U.S. manufacturers to ensure sufficient stocks of broadspectrum antibiotics ahead of licensing them for animal feeds. Pouncing on the opportunity to expand sales of its chlortetracycline feed AURO-FAC2A, American Cyanamid's Lederle Laboratories Division offered free Aureomycin (chlortetracycline) and the expertise of antibiotic growth effect co-discoverer Thomas Jukes. Lederle's director hoped that the arrangement would "be the beginning of an association which will be of mutual benefit."<sup>29</sup>

Public support for AGPs was mixed. On the one hand, *Times* articles heralded AGPs as a "strange nutrition" with the potential to solve the "world-wide shortage of protein."<sup>30</sup> On the other hand, readers of the *Observer* engaged in a heated exchange regarding the practice.<sup>31</sup> The pro-

23. TNA MAF 287/299 (BVA to Lambert, July 15, 1953).

24. TNA MAF 119/23 (Honnor, ARC Meeting, September 19, 1952), 3.

25. TNA MAF 119/23 (Magee; ARC Meeting, February 25, 1952); MAF 119/23 (ARC Meeting, September 19, 1952), 1.

26. TNA MAF 119/23 (W. G. Alexander; ARC Meeting, February 25, 1952), 2.

27. TNA MAF 287/299 (R. Braude; Meeting at Saughton to discuss TSA draft regulations, February 4, 1953), 3.

28. TNA MAF 287/299 (Veterinary Interests, Meeting RCVS and BVA with MH and MAF, February 12, 1953).

29. TNA MAF 287/299 (Williams to Moss, February 5, 1953), 2.

30. G. R. H. Nugent, "The Twentieth-Century Hen," Times, July 30, 1951, 5.

31. Olive Whicher, "Penicillin for Pigs," *Observer*, November 28, 1952, 2; G. Pelham Reid, "Guidance Required," *Observer*, January 4, 1953, 3; J. A. Wakelam, "Penicillin for Pigs," *Observer*, January 4, 1953, 3.

posed TSA was also attacked in Parliament: in February 1953, Labour and Co-op MP Norman Dodds asked the Minister of Agriculture how consumers could be safeguarded while "famous experts . . . declared that more harm than good" would result from AGPs.<sup>32</sup> Seconding Dodd's question, Conservative MP Colonel Alan Gomme-Duncan asked "whether we have all gone mad to want to give penicillin to pigs to fatten them? Why not give them good food, as God meant them to have."<sup>33</sup>

British farmers' attitudes toward antibiotics were also mixed. Some of the reasons for this were disappointing antibiotic feed trials, the availability of cheap alternative sources of vitamin B12, and varying degrees of intensification in different livestock sectors.<sup>34</sup> While Britain's poultry industry intensified rapidly and quickly adopted the routine use of antibiotics and sulphonamides during the 1950s,<sup>35</sup> intensification and antibiotic use among pork producers was more piecemeal because of smaller and more diverse farms and a preference for outdoor rearing.<sup>36</sup> Similarly, British cattle producers partially adopted intensive antibiotic dependent rearing methods only around 1960 following the integration of West Country dairy regions with Eastern grain-producing areas for the fattening of calves.<sup>37</sup>

Wary of the advertised efficacy of the new miracle feeds ahead of the 1953 TSA, the NFU lobbied for guaranteed minimum antibiotic concentrations in feeds and official security guidelines.<sup>38</sup> However, the NFU lacked internal expertise. As a consequence, enthusiastic government experts played a significant role in winning Britain's farming establishment over to "modern" feeding practices. Following a joint meeting in 1953, the NFU's representative thanked officials: "The subject was one

32. TNA MAF 287/299, Extract, House of Commons (P.Q. 3355), question put on February 19, 1953 (Pig Fattening).

33. Ibid.

34. Claas Kirchhelle, *Pyrrhic Progress. Antibiotics in Anglo-American Food Production* (forth-coming with Rutgers University Press); see also Berdah, "One Health" (n. 20).

35. Andrew Godley and Bridget Williams, "Democratizing Luxury and the Contentious 'Invention of the Technological Chicken' in Britain," *Bus. Hist. Rev.* 83 (2009): 267–90.

36. Abigail Woods, "Rethinking the History of Modern Agriculture: British Pig Production, c. 1910–65," *Twent. Cent. Brit. Hist.* 23, no. 2 (2012): 165–91, quotation on 165; see also ongoing work by Alex Bowmer.

37. TNA MAF 287/199 (Cattle Dealing and Salmonellosis), 1; Extract: "Diseases Master Drug Defences," *Farmers Weekly*, May 19, 1967; Extract: Williams Smith, "Salmonella," *Farmers Weekly*, January 13, 1967, 87.

38. TNA MAF 287/299 (Dugdale to Turner, July 29, 1953), 1; (Draft Regulation Therapeutic Substances Bill, Meeting, July 3, 1953).

about which he and many other farmers were relatively ignorant and he was grateful for the information and advice given. He was in general agreement . . . , but felt that caution in propaganda and in the use of antibiotics was necessary for the time being."<sup>39</sup>

Despite farmers' initial wariness, the 1953 licensing of penicillin and Aureomycin AGPs for pigs and poultry was a commercial success. Regardless of the size of their farms, British farmers invested in antibiotics: while an estimated 69,439 tons of supplemented feeds were sold in 1954, the number had risen to 445,706 tons in 1959—antibiotic supplements for home mixing not included.<sup>40</sup> In 1958, veterinary researcher Herbert Williams Smith estimated that "about 50% of all the pigs in Britain are so fed and that nearly all unweaned piglets have access to food containing tetracyclines."<sup>41</sup> By 1963, approximately 44% of British antibiotics were consumed by animals.<sup>42</sup> While antibiotics played a particularly prominent role in British poultry, turkey, and game bird production,<sup>43</sup> antibiotic mastitis treatments facilitated productivity increases in dairy husbandry and antibiotic feeds nurtured rising numbers of piglets and calves.<sup>44</sup> With antibiotic dosages in feeds increasing, the boundaries between growth promotion, prophylaxis, and treatment soon blurred.<sup>45</sup>

Officials actively encouraged agricultural antibiotic use but had few tools with which to control it. Already recognized by contemporaries, Britain lacked analytical facilities for detecting and measuring the concentration of agricultural drugs and chemicals in feeds, food, or the environ-

39. TNA MAF 287/299 (G. Hedley; Meeting at Saughton to discuss TSA draft regulations, February 4, 1953), 4.

40. TNA FD 1/8226 (Office Note observations on aspects of the use of antibiotics supplied by the CAFSMNA [ARC 574/60]), 1.

41. Herbert Williams Smith, "Drug-Resistant Bacteria in Domestic Animals [Presentation: 'Symposium on Epidemiological Risks of Antibiotics,' February 21, 1958]," *Proc. Roy. Soc. Med.* 51, no. 10 (1958): 812–13, quotation on 812.

42. Joint Committee on the Use of Antibiotics in Animal Husbandry and Veterinary Medicine, *Report: Joint Committee on the Use of Antibiotics in Animal Husbandry and Veterinary Medicine* (London: HMSO, 1969), 65–66.

43. John Martin, "The Commercialisation of British Turkey Production," *Rural Hist.* 20, no. 2 (2009): 209–28, quotation on 209–10; Martin, "The Transformation of Lowland Game Shooting in England and Wales since the Second World War: The Supply Side Revolution," *Rural Hist.* 22, no. 2 (2011): 207–26, quotation on 207; Godley and Williams, "Democratizing Luxury" (n. 35).

44. Woods, "Science" (n. 10,) quotation on 294.

45. TNA MAF 189/911 (Some Problems with the Use of Antibiotics in Poultry Husbandry in Great Britain ARC 156/58); Williams Smith, "Drug-Resistant Bacteria in Domestic Animals" (n. 41), 812.

ment.<sup>46</sup> For data on residues, British regulators depended on academic publications and foreign enforcement agencies. Meanwhile, enforcement of the TSA remained confined to retail-level inspections by the Pharmaceutical Society of Great Britain.<sup>47</sup> As a consequence, authorities had no way of prohibiting farmers—or veterinarians—from using legally purchased antibiotics as they pleased.<sup>48</sup> While the 1953 TSA opened the floodgates for a national public health experiment, the authorities tasked with controlling this experiment were flying blind.

The updated TSA of 1956 did not remedy the situation. Attempting to regulate therapeutic substances comprehensively, the act was divided into two parts: while Part I dealt with licensing, manufacture, and the importation of medications, Part II listed substances to be sold on prescription only-among them penicillin and the tetracyclines. Mirroring its predecessor, the 1956 TSA allowed ministers to relax Part II in the case of low-dose AGPs.<sup>49</sup> The act contained a further significant loophole by not automatically assigning a prescription-only scheduled status to new substances. It was thus possible to sell unscheduled drugs directly to consumers. Such sales occurred in the case of tylosin, an antibiotic initially considered therapeutically irrelevant.<sup>50</sup> Instead of closing this loophole, legislators remained sanguine. As Alfred Louis Bacharach, former chief executive scientific officer at Glaxo Laboratories, put it in 1957, manufacturers and MAFF regulated unscheduled substances according to a "gentleman's agreement"<sup>51</sup>—an arrangement that was later codified in the voluntary Veterinary Products Safety Precautions Scheme. Similar to the agricultural sector, corporatist ties between Whitehall and the pharmaceutical industry resulted in industrial self-regulation and laissez-faire drug legislation.52

While antibiotic enforcement withered, expert committees bloomed. Because of antibiotics' numerous uses, a veritable jungle of committees became concerned with their use. Originally, the Medical and Agricultural Research Councils had given advice regarding agricultural antibiotics to MAFF and the MH. Soon, further committees started concerning them-

46. TNA MAF 119/23 (Eden to Robertson, November 2, 1953), 2.

47. TNA MAF 119/23 (Dee to Hammence, July 3, 1958), 1-2.

48. TNA MAF 287/299 (Meeting at Saughton regarding TSA draft regulations, February 4, 1953), 1.

49. TNA MAF 119/23 (Draft: F. G. Raymond to G. L. Gray, November 26, 1968).

50. TNA MAF 284/281 (Minute 27, A. B. Bartlett, April 10, 1956).

51. A. L. Bacharach, "UK Position on Use of Antibiotic Food Additives," *Chemical Age* 78 (1957): 176.

52. TNA MAF 284/281 (Control of Antibiotics, February 1969), 1.

selves with the subject. Among them were the Preservatives Sub-Committee of the Food Standards Committee and the Scientific Sub-Committee of the Advisory Committee on Poisonous Substances Used in Agriculture and Food Storage. In turn, these two committees founded a joint Antibiotics Panel in 1956.<sup>53</sup>An additional expert body was later set up by the Milk Marketing Board. Unsurprisingly, the numerous committees vied for influence and frequently disagreed. As a result, departmental and expert responsibilities blurred and there was no guiding principle driving British antibiotic policy. By 1967, an official complained that he was "quite unable to understand the relationship between these bodies."<sup>54</sup> His colleagues agreed: "The situation is now so complicated that it is almost un-understandable."<sup>55</sup>

Meanwhile, the list of permitted antibiotic applications grew rapidly. In 1954, the Therapeutic Substances (Supply of Oxytetracycline for Agricultural Purposes) Regulations legalized the use of oxytetracycline AGPs. Four years later, streptomycin and oxytetracycline sprays and paint solutions for horticultural purposes were permitted in Britain. In 1964, the field of antibiotic use was extended to the preservation of fish with Aureomycin ice and dipping solutions.<sup>56</sup>

Retrospectively, this carefree attitude regarding antibiotics may seem bizarre, especially since it occurred during a time of growing warnings about antibiotic allergies and resistance in medical settings.<sup>57</sup> In Britain, lax contemporary attitudes can be explained by four factors: The first and decisive factor was the theory that natural bacterial resistance or resistance arising through spontaneous mutations spread only in a hereditary fashion from one generation to the next. This hereditary ("vertical") concept of resistance proliferation made experts confident that resistance selection on farms presented a localized problem, which would disappear via competitive inhibition after discontinuing antibiotic use.<sup>58</sup> The second

54. TNA MAF 287/450 (Minute, Hensley to Bott, January 9, 1967).

55. TNA MAF 287/450 (Minute, Macrae to Field, January 18, 1967), 2; TNA MAF 287/450 (Minute, Field to Macrae, January 23, 1967), 2.

56. TNA MAF 284/282 (Control of Antibiotics, Appendix III: List of relaxing regulations made under Part II of the therapeutic Substances Act 1956, February 1959).

57. Podolsky, Antibiotic Era (n. 3), 141-42.

58. Christoph Gradmann, "Sensitive Matters: The World Health Organisation and Antibiotic Resistance Testing, 1945–1975," *Soc. Hist. Med.* 23, no. 3 (2013): 555–74, quotation on 556–60; Scott H. Podolsky et al., "History Teaches Us That Confronting Antibiotic Resistance Requires Stronger Global Collective Action," *J. Law Med. Ethics* 43, no. 3 (2015): 27–32, quotation on 27.

<sup>53.</sup> TNA MAF 101/643 (Note of Meeting on September 13, 1956, to discuss the setting up of a Working Group on the use of Antibiotics in Agriculture and in Food Preservation).

factor behind official complacency was Britain's ongoing lack of analytical facilities. Unwilling to finance expensive surveillance, the extent of antibiotic residue and resistance problems remained invisible. The third factor was the close corporatist relationship between officials and industry. Once made, gentlemen's agreements were hard to break. The fourth factor was a certain national pride of a regulatory system that was cheaper than that of the United States, where authorities were trying to establish antibiotic residue limits in food.<sup>59</sup>

# Linking the Farm and the Hospital—Phage-Typing and the PHLS

By the late 1950s, bacteriological research undermined both haphazard antibiotic regulations and the distinction between resistance selection in hospitals and on farms. This research was enabled by the PHLS's unprecedented centralization of British bacteriological networks and a technology called phage-typing. Phage-typing uses bacteriophages—viruses that infect only bacteria—to identify ("type") individual bacteria strains. Since the 1930s, the PHLS had developed international phage-typing sets for *Salmonella typhi, Salmonella paratyphi, Salmonella typhimurium*, and *Staphylococcus aureus*. By the 1950s, researchers at PHLS headquarters in Colindale were mapping bacteria strains at the regional, national, and international levels.<sup>60</sup> Once they became interested in antibiotic resistant strains, supposed distinctions between medical and agricultural resistance selection blurred.

A significant factor contributing to this blurring of human-animal boundaries was intensive cooperation between the PHLS and veterinary authorities. After 1945, the PHLS offered training courses and phage-typing sets to interested researchers across Britain.<sup>61</sup> One of the first veterinary researchers to fully embrace phage-typing was Herbert Williams Smith, who had briefly worked for the PHLS during the 1940s. Based at the Animal Health Trust in Stock,<sup>62</sup> Williams Smith devised phage-typ-

59. TNA MAF 260/82 (Western European Union Sub-Committee on Health Control of Foodstuffs. Working Party on Poisonous Substances Used in Agriculture; Draft by UK Delegation, 1956), 6–7.

60. R. E. O. Williams, Microbiology for the Public Health: The Evolution of the Public Health Laboratory Service 1939–1945 (London: PHLS, 1985), 21–22, 45.

61. TNA MAF 189/390 (C. D. Spencer to J. A. Aldrige, August 31, 1954).

62. Naomi Datta, "Herbert Williams Smith. 3 May 1919–16 June 1987," *Biog. Mem. Fellows Roy. Soc.* 34 (1988): 754–86, quotation on 754.

ing systems for staphylococci and *Escherichia coli* from animal sources.<sup>63</sup> Together with his collaborator W. E. Crabb, he presented a paper on AGPs' effects on antibiotic resistance in *E. coli* from pig and chicken feces at the 1956 Veterinary Congress. Noting that they had had great difficulty in finding control animals from farms where antibiotics were not used, the authors identified a significant correlation of antibiotic use and resistance. They warned that resistance selection in animals "would undoubtedly have an impact on the treatment of *bact. Coli* infection in those animals and possibly other species, including man, with which they come in contact. It is apparent that considerations of this nature should be given very serious thought before any chemotherapeutic agent is permitted to be used in such a widespread manner as the tetracyclines have been used in pig nutrition."<sup>64</sup> AGPs' low dosage and continuous use seemed particularly likely to select for resistance.<sup>65</sup>

Between 1958 and 1960, Williams Smith and Crabb linked resistance selection in animals and humans. In 1960, a paper in the *Journal of Pathology and Bacteriology* compared staphylococci samples of 160 pigs fed tetracycline additives to a control group fed without antibiotics. Of the pigs fed tetracyclines, 67 percent carried *S. aureus* strains resistant to tetracyclines. Of 50 attendants caring for tetracycline- and penicillin-fed chickens, 30 percent carried penicillin-resistant *S. aureus*, 14 percent tetracycline-resistant *S. aureus*, and 4 percent penicillin- and tetracycline-resistant *S. aureus*. Phage-typing showed that resistant bacterial strains carried by attendants and animals were largely identical.<sup>66</sup>

63. Herbert Williams Smith and W. E. Crabb, "The Sensitivity of a Further Series of Strains of *Bacterium coli* from Cases of White Scours: The Relationship between Sensitivity Tests and Response to Treatment," *Vet. Rec.* 68 (1956): 274–77, quotation on 274; Smith and Crabb, "The Typing of *Escherichia coli* by Bacteriophage: Its Application in the Study of the *E. coli* Population of the Intestinal Tract of Healthy Calves and of Calves Suffering from White Scours," *J. Gen. Microbiol.* 15 (1956): 556–74, quotation on 556.

64. Smith and Crabb, "The Effect of the Continuous Administration of Diets Containing Low Levels of Tetracyclines on the Incidence of Drug-Resistant *Bacterium coli* in the Faeces of Pigs and Chickens: The Sensitivity of the Bact. coli to Other Chemotherapeutic Agents," *Vet. Rec.* 69 (1957): 24–30, quotation on 24.

65. Grave warnings about agricultural AMR selection had been voiced by several U.S. veterinary bacteriologists as early as 1951. However, the absence of systematized national bacteriological surveillance prevented early U.S. research from being expanded. Williams Smith seems to have been unaware of the earlier U.S. papers: Mortimer P. Starr and Donald M. Reynolds, "Streptomycin Resistance of Coliform Bacteria from Turkeys Fed Streptomycin," *Amer. J. Pub. Health* 41, no. 11 (1951): 1375–80, quotation on 1377.

66. Herbert Williams Smith, "The Effect of Diets Containing Tetracyclines and Penicillin on the Staphylococcus Aureus Flora of the Nose and Skin of Pigs and Chickens and Their Meanwhile, PHLS researchers began to look for resistance development in other bacterial organisms. Their results indicated that *S. typhimurium* strains isolated from British poultry were also becoming resistant to feed antibiotics.<sup>67</sup> Although scenarios of vertical resistance proliferation continued to dominate discussions, phage-typing data on the spread of resistant strains of well-known pathogens posed a challenge to antibiotic use on British farms. In 1959, the ARC referred to the still unpublished PHLS *S. typhimurium* study to insist on a critical reassessment of all AGPs.<sup>68</sup> Taken aback by the potential implications of antibiotic withdrawals for agricultural practice, an internal minute marveled: "[The ARC] are considering putting the clock back."<sup>69</sup>

## Entangled Reform—The Power Struggles over Antibiotic Regulation

In April 1960, a Joint ARC/MRC Committee on Antibiotics in Animal Feeding began to reevaluate existing regulations in the light of the new evidence on antibiotic resistance proliferation.<sup>70</sup> Chaired by the retired NFU president, Sir James Turner—now Lord Netherthorpe—the so-called Netherthorpe Committee's incorporation of agricultural, veterinary, and medical interests was a classic example of corporatist decision making. The committee's main body met only twice. During its first meeting in 1960, it installed a scientific subcommittee. Two years later, it endorsed the subcommittee's report.<sup>71</sup>

The subcommittee itself met five times between 1960 and 1962. However, behind closed doors, it soon became apparent that a fundamental rift divided members. While one faction consisting mostly of medical and veterinary experts attacked AGPs because of their selection for bacterial resistance, the other faction consisting of agricultural scientists and officials fiercely defended AGPs because of their economic benefits. The

Human Attendants," *J. Pathol. Bacteriol.* 79, no. 2 (1960): 243–49, quotation on 243; "Drug-Resistant Staphylococci in the Farmyard," *Lancet* 275 (1960): 1338–39.

<sup>67.</sup> B. C. Hobbs et al., "Antibiotic Treatment of Poultry in Relation to Salmonella Typhi-Murium," Mon. Bull. Minist. Health Pub. Health Lab Serv. 19 (1960): 178–92.

<sup>68.</sup> TNA FD 9/1458 (Porter to Clements, July 17, 1959).

<sup>69.</sup> TNA FD 9/1458 (Note on file, A.83/4, September 9, 1959).

<sup>70.</sup> TNA FD 9/1458 (Minute, Faulkner, March 7, 1960).

<sup>71.</sup> TNA FD 23/1936 (Report of the Joint Committee on Antibiotics in Animal Feeding, 1962).

committee's clashes reflected a wider conflict within the animal health sector: as a result of the contemporary shift to mass animal health management and the treatment of nonspecific diseases, animal nutritionists favored unfettered access to antibiotics. Meanwhile, British veterinarians were keen to assert their authority over animal health management and preventive health care and advocated lucrative prescription-only access to antibiotics.<sup>72</sup>

In virtually every meeting, the heads of the respective factions, Robert Fraser Gordon (veterinarian) and Raphael Braude (animal nutritionist), clashed on the relative costs and benefits of low-dosed AGPs. When Herbert Williams Smith was invited to give evidence in June 1960, he presented new data on the spread of antibiotic resistance to humans: in one survey, 88.3 percent of *Staphylococcus aureus* isolates from the noses of veterinary surgeons and farmers were penicillin-resistant. Of isolates from veterinarians, 14.7 percent were also resistant to the antibiotic chloramphenicol.<sup>73</sup> According to Williams Smith, even low levels of antibiotic use could select for bacterial resistance.<sup>74</sup> In response, Braude asked for conclusive evidence of actual harm resulting from resistant bacteria on farms. Williams Smith conceded that he was unable to supply such evidence. The subcommittee therefore compromised on the statement that antibiotic use "could lead to the production of resistant strains, . . . the dangers of uncontrolled therapeutic use should be born in mind."<sup>75</sup>

Remarkably, NFU evidence showed that problematic antibiotic use was indeed taking place on farms. Contradicting the benign picture painted by Braude, the NFU submission contained three farmers' statements. One farmer confessed having used antibiotics illegally to feed breeding pigs.<sup>76</sup> A second farmer reported "certain instances where high-level doses of antibiotics have been used in an attempt to offset bad husbandry practices."<sup>77</sup> The subcommittee's minutes poignantly noted "the difference of opinion

72. Woods, "Is Prevention Better Than Cure?" (n. 7), 113; also see Fortané, "Foundation of the Swine Pathology Station in Ploufragan" (n. 8); Thoms, "Handlanger der Industrie oder berufener Schützer des Tieres?" (n. 7).

73. TNA FD 1/8226 (ARC/MRC Joint Committee on Antibiotics, the Antibiotic Sensitivity of Strains of Staphylococcus aureus Isolated from the Noses of Veterinary Surgeons and Farmers, Williams Smith & Crabb).

74. TNA FD 1/8226 (ARC/MRC Joint Committee on Antibiotics, 2nd meeting Scientific Subcommittee, June 27, 1960), 2.

75. Ibid., 3.

76. TNA FD 1/8226 (Information provided by the NFU, ARC 558/60), 1.

77. Ibid., 2.

between the farming members of the Joint Committee and the farmers whose opinion had been put forward as representative by the NFU."<sup>78</sup>

In view of the disagreement between medical and agricultural members, the Netherthorpe subcommittee soon reached an impasse. Acknowledging this impasse, University of Glasgow bacteriologist and soon-to-be PHLS director James Howie presented members with three choices:

1. Complete prohibition of the addition of antibiotics to feedingstuffs (i.e., a reversion to the earlier situation, which would be very difficult)

2. Maintenance of the present position (on the ground that the conflicting evidence did not provide any basis for a change)

3. General permission to add antibiotics to feeding stuffs (on the ground that there was insufficient evidence to justify the with holding of such permission)<sup>79</sup>

Howie's phrasing was significant. By presenting only three choices—two of which were extremes—he transformed the status quo ante into an acceptable compromise. Both factions could subsequently claim to have prevented worse.

Yielding to Braude's objections, the subcommittee agreed that contemporary evidence was insufficient to warrant AGP restrictions. Retrospectively legalizing a common practice, the subcommittee further recommended an extension of AGPs to calves but blocked a suggested extension to layer birds and adult stock. Both factions further agreed on the necessity of antibiotic and resistance monitoring. Most significantly, the medical faction pushed through a recommendation that new antibiotics should be licensed for use as AGPs only on the basis of their irrelevance to human and animal therapy.<sup>80</sup>

The suggested distinction between therapeutic and nontherapeutic antibiotics was not new: the Antibiotics Panel had discussed it in 1956.<sup>81</sup> However, by inserting a two-tier licensing system into the subcommittee's report, the medical faction scored a significant victory. Changed licensing procedures would promote the development of seemingly harmless nontherapeutic AGPs. Over time, nontherapeutic products would make popular penicillin- and tetracycline-based AGPs expendable. According to contemporary theories of vertical resistance proliferation, withdraw-

81. TNA MAF 284/281 (Advisory Committee on Poisonous Substances, Meeting, November 13, 1956; minutes Antibiotics Panel, comment Barnes).

<sup>78.</sup> TNA FD 1/8226 (ARC/MRC Joint Committee on Antibiotics, 3rd meeting Scientific Subcommittee, October 18, 1960), 4.

<sup>79.</sup> Ibid., 5.

<sup>80.</sup> TNA FD 1/8227 (ARC/MRC Joint Committee on Antibiotics in Animal Feeding, Report of the Scientific Subcommittee).

ing these antibiotics would reduce corresponding levels of bacterial resistance.  $^{\rm 82}$ 

The introduction of a two-tiered licensing system and the gradual reservation of medically relevant antibiotics was also a perfect example of compromise-oriented corporatist boundary work: higher-dosed veterinary prescriptions of new therapeutic antibiotics would not be prohibited and general nonhuman antibiotic use would be safeguarded by classifying nontherapeutic AGPs as safe. It seemed as though the demands of farmers, veterinarians, and public health experts could all be satisfied.

However, regulators soon found that the 1962 Netherthorpe report failed to reassure the public. In Britain, the 1960s witnessed significant criticism of agricultural antibiotic use. Between 1962 and 1964, the British public was sensitized to the issues of chemical residues, antibiotic resistance, and animal cruelty on so-called factory farms by a national milk scandal (1962), the publication of Rachel Carson's *Silent Spring* (1963, U.K.),<sup>83</sup> and Ruth Harrison's *Animal Machines* (1964).<sup>84</sup> Meanwhile, agricultural antibiotics also emerged as a prominent concern of the rejuvenating organic movement.<sup>85</sup>

Public pressure for large-scale antibiotic reform peaked in 1965 when a paper in the *Lancet* challenged established resistance proliferation models. Authored by Naomi Datta and Ephraim Saul "Andy" Anderson, director of the PHLS's Enteric Reference Laboratory, the paper discussed interbacterial ("horizontal") resistance transfer in resistant *S. typhimurium* and in vitro transfer of ampicillin resistance to previously sensitive strains of *S. typhimurium* and *E. coli*. It had emerged that bacteria not only were able to vertically inherit genes encoding for antibiotic resistance but could also communicate them among each other by exchanging extrachromosomal DNA fragments called plasmids.<sup>86</sup> The fact that bacteria could exchange genetic information was not new in itself. In 1946, Joshua Lederberg and Edward Tatum had already observed bacterial conjugation. Working

82. Temporary penicillin restrictions by Mary Barber were cited by experts like Ernst Boris Chain in defense of AGPs. Wellcome Collection Personal Papers E. B. Chain G 72 (The Problem of the Emergence of Bacterial Resistance to Antibiotics, April 10, 1967), 8.

83. Rachel Carson, *Silent Spring*, 50th anniversary ed. (New York: First Mariner Books, 2002).

84. Ruth Harrison, Animal Machines (London: Vincent Stuart, 1964).

85. Robert Bud, *Penicillin: Triumph and Tragedy* (Oxford: Oxford University Press, 2009), 171–76; Kirchhelle, "Pyrrhic Progress" (n. 19), 5.

86. E. S. Anderson and Naomi Datta, "Resistance to Pencillins and Its Transfer in Enterobacteriaceae," *Lancet* 285 (1965): 407–9. on *Shigella* during the 1950s, Tsutomu Watanabe discovered that plasmids could also encode genetic instructions on how to resist antibiotics (so-called R-factors).<sup>87</sup> What was new about Anderson and Datta's 1965 paper was that horizontal resistance transfer also occurred in nonhuman settings and could potentially cross over from bacteria in animal populations to those in humans. Popularized amid growing general environmentalism, horizontal—or "infective"—resistance transfer further eroded the supposed divide between resistance selection in agricultural and medical settings.

Concerns about "factory farming" and horizontal resistance transfer fundamentally undermined the corporatist safety compromise of the 1962 Netherthorpe report. E. S. Anderson emphasized the threat posed by resistance selection on farms in a series of high-level attacks on agricultural antibiotic use. Three months after his initial plasmid article, he published a paper in *Nature* on rising levels of resistant *S. typhimurium* phage Type 29 and blamed them on the "infective hazards of intensive farming."<sup>88</sup> In December 1965, he published another article in the *British Medical Journal*. Having analyzed numerous Type 29 *S. typhimurium* samples of human and animal origin, Anderson found many of them resistant to furazolidone, a drug used exclusively in veterinary medicine.<sup>89</sup>

Anderson's warnings received widespread media attention.<sup>90</sup> As Robert Bud has shown, Anderson embodied a new type of public expert, whose vocal nature challenged the club-like atmosphere of corporatist expert consultation.<sup>91</sup> Later described as "a hard taskmaster" with an "abrasive and perfectionist approach,"<sup>92</sup> Anderson was able to raise awareness about "infective resistance" by cultivating friendships with the *Guardian*'s Anthony Tucker and Bernard Dixon, future editor of the *New Scientist*. However, his public partisanship for antibiotic restrictions came at a price. Although he successfully pushed for a new AGP review, Anderson's departure from the confidential and compromise-oriented corporatist

87. Podolsky, Antibiotic Era (n. 3), 141-42, 154-56; Bud, Penicillin (n. 85), 175.

88. E. S. Anderson and M. J. Lewis, "Drug Resistance and Its Transfer in *Salmonella Typhimurium*," *Nature* 206 (1965): 579–83, quotation on 583.

89. E. S. Anderson, "Origin of Transferable Drug-Resistance Factors in the Enterobacteriaceae," *Brit. Med. J.* 2, no. 5473 (1965): 1289–91, quotation on 1289.

90. "Germ Survival in Face of Antibiotics," *Times*, February 26, 1965, 15; "New Health Fear on Super-Farms," *Observer*, November 28, 1965, 5; "Warning on Factory-Farm Bacteria," *Observer*, January 30, 1966, 4.

91. Bud, Penicillin (n. 85), 177-78.

92. Anthony Tucker and John Threlfall, "Obituary: E. S. Anderson," *Guardian*, March 22, 2006.

fold reduced his influence on the direction of official antibiotic boundary work.

In spring 1965, the British government reacted to public and scientific pressure by recalling the Netherthorpe scientific subcommittee. Asked to give evidence and later accused of instigating the whole committee,93 Anderson passionately argued for antibiotic restrictions. Surveilling antibiotic resistance in S. typhimurium since 1961, Anderson's team had identified a dramatic rise of increasingly resistant salmonellosis outbreaks caused by S. typhimurium Type 29. Whereas 16.7 percent of Type 29 isolates were antibiotic resistant in November 1964, the proportion of resistant strains had risen to 59.8 percent in April 1965. Worryingly, Type 29's resistance spectrum had also increased: In 1963, the team had discovered Type 29 strains with resistance against sulphonamides and streptomycin. Tetracycline resistance was detected in early 1964. By June 1964, most Type 29 cultures were resistant to all three drugs. Ampicillin resistance appeared three months later. Significantly, Type 29's streptomycin, sulphonamide and ampicillin resistance was plasmid-encoded and transferable. Using any antibiotic on Type 29's resistance spectrum would automatically select for resistance against all of the other antibiotics.94 Writing in support of Anderson, Herbert Williams Smith reported that his team had analyzed two Type 29 outbreaks that had also proven resistant to neomycin and furazolidone-drugs not included in Anderson's resistance surveillance.95

	Total S. typhimurium	Total Type 29	Origin			
			Human		Animal	
Year			Total	Drug- resistant	Total	Drug- resistant
1961–62	882	9	8	0	1	0
1962-63	926	6	5	1	1	0
1963-64	825	91	11	11	80	76
1964 - 65	2,109	800	151	146	649	638

Table 1. Cultures of *S. typhimurium* Phage Type 29 Examined in the Enteric Reference Laboratory in Six-Month Periods, November 1–April 30

Source: TNA FD 1/8228—The Increase of Drug Resistance in S. typhimurium (June 1965)

93. TNA MAF 287/450 (Minute, Macrae to Field, January 18, 1967), 1.

94. TNA FD 1/8228 ARC 413/65—The Increase of Drug Resistance in S. typhimurium (June 1965).

95. TNA FD 1/8228 Note by Williams Smith (ARC443/65).

PHLS and veterinary investigations soon linked the increase of Type 29 outbreaks to new intensive rearing practices for male calves. These calves were no longer slaughtered after birth in the dairy regions of the West Country but were being sold for fattening to producers in the grainrich Eastern part of England. The calves were often less than one week old and particularly susceptible to salmonella infections. Often held and transported in unhygienic settings, the young calves were treated with a whole barrage of antibiotics to keep infections at bay. Remarkably, PHLS phage-typing enabled investigators to trace most of the resistant Type 29 outbreaks to the premises of one Sussex calf dealer. This dealer resisted official hygiene advice and had used lax drug laws and veterinary prescriptions to market calves together with six-week feeding kits containing many of the antibiotics to which Type 29 had developed resistance. Despite their concerns, there was nothing officials could do to stop either the dealer or his antibiotic suppliers from continuing this practice.<sup>96</sup>

For Anderson, officials' impotence and the rapid spread of Type 29 posed a fundamental challenge to agricultural antibiotic use. In its 1962 report, the Netherthorpe Committee had conceded that agricultural antibiotics were selecting for resistance in Salmonella and E. coli but had emphasized that resistance selection was restricted to the antibiotic in use. According to Anderson, this was no longer true: "Multiple resistance is now the rule.... I have already pointed out that the use of any drug in a multiple spectrum of resistance protects the entire spectrum, so that, for example, resistances to ampicillin, streptomycin, sulphonamides, neomycin, kanamycin, and furazolidone will all flourish under the umbrella of tetracycline if they are associated with resistance to that drug."97 In front of the committee, Anderson argued that because it was unclear whether resistance would "die out in an animal population if the use of antibiotics was discontinued," quick action was imperative lest "the situation be irreversibly changed."98 Since resistance development occurred in jumps, it was not inconceivable that transferable resistance to chloramphenicol—a vital drug against typhoid—might soon emerge. Meanwhile, the widespread use of tetracycline and penicillin AGPs was

96. TNA MAF 287/199 (Cattle Dealing and Salmonellosis), 1; Extract: "Diseases Master Drug Defences," *Farmers Weekly*, May 19, 1967; Extract: Williams Smith, "Salmonella," *Farmers Weekly*, January 13, 1967, 87; TNA FD 1/8228 (ARC/MRC Committee in Animal Feeding. Scientific Subcommittee December 13, 1965), 3.

97. TNA FD 1/8228 (E. S. Anderson-Comments on ARC 561/65).

98. TNA FD 1/8228 (ARC/MRC Committee in Animal Feeding. Scientific Subcommittee June 22, 1965), 1.

creating a perfect environment for the proliferation of antibiotic resistance. Stressing the paradigm-shifting implications of horizontal gene transfer, Anderson noted: "the position was that R-factors now have an epidemiology of their own, covering transfer between strains and species and also between hosts."<sup>99</sup>

Asked what steps he would take if he were given dictatorial powers, Anderson argued for the following:

1. Prohibition for a time of the use of antibacterial drugs as food additives or preventatives

2. Restriction of the therapeutic use of such drugs to cases where they were justified on bacteriological evidence

3. A decision to be made as to which antibiotics could usefully continue to be employed

4. No drug likely to be useful in human medicine to be used in animal rearing
5. No drug likely to be useful in veterinary medicine to be used as a feed additive<sup>100</sup>

Anderson also argued for improved salmonellosis follow-ups, antibiotic advertising restrictions, improved animal husbandry, and enhanced resistance surveillance.

Unsurprisingly, these recommendations proved controversial within the scientific subcommittee, whose terms of reference limited it to assessing AGPs. Despite admitting that farmers were routinely feeding subtherapeutic and therapeutic antibiotic doses to calves, agricultural experts argued that "the use of most of the antibiotics discussed was illegal without a veterinary prescription"<sup>101</sup> and therefore beyond the committee's purview. Meanwhile, the committee's old impasse regarding already licensed AGPs remained in place. In June 1965, the reconvened committee therefore merely called for more research and reconfirmed existing regulations—including the planned licensing of AGPs for calves.<sup>102</sup>

For Anderson, this decision was unacceptable. In December 1965, a second recall of the Netherthorpe Committee was prompted when PHLS director Howie withdrew "his concurrence in the recommendations of the [June 1965] draft report."<sup>103</sup> New evidence by Anderson had strengthened the case against both low-dosed AGP-use and high-dosed antibiotic pro-

103. TNA FD 1/8228 (ARC/MRC Committee in Animal Feeding. Scientific Subcommittee Meeting on December 13, 1965. Brief), 1.

<sup>99.</sup> Ibid., 2.

<sup>100.</sup> Ibid., 1–2.

<sup>101.</sup> Ibid., 2.

<sup>102.</sup> Ibid., 4–5.

phylaxis. Presenting a "phylogeny" of resistance development, Anderson argued that constant selection for mutational Type 29 tetracycline resistance had created an umbrella for the rise of plasmid-encoded resistance against numerous other drugs. Despite having identified a lab strain of Type 29 in which tetracycline resistance was not mutational but encoded as an R-factor—which Anderson designated T"—Anderson's team had previously thought that transferable tetracycline resistance was rare. Recently, however, they had found an R-factor indistinguishable from T" in Type 29 S. typhimurium that had been isolated from a herd of pigs. In the case of the lab-identified T", It was possible to infect "almost 100% of recipient cells of either S. typhimurium or Escherichia Coli K12 [with plasmid-encoded] R-factors] after overnight contact with a donor strain."<sup>104</sup> Although the porcine Type 29 strain had not spread outside the closed herd, it was possible that T" might escape into the wider environment via E. coli, which were not being monitored for. In sum, Anderson's findings suggested that constant high- and low-dosed selection for tetracycline resistance was more important for "the present situation in drug resistance in S. typhimurium than was realized earlier."105

With experts openly disagreeing about the implications of Anderson's evidence, it was, however, apparent that the Netherthorpe subcommittee would not be able to reform AGP use. Fortunately, Anderson's focus *on S*. typhimurium in calves had an unforeseen consequence. Because AGPs had not yet been legalized for calves, penicillin and tetracycline resistance in bacteria isolated from calves logically resulted either from illegal AGP use or from veterinary over-prescription. Endorsing Anderson's call for an expert review of all antibiotics, committee members thus shifted their focus from farmers to veterinary prescription practices. In its subsequent draft report, the subcommittee called for a new expert committee to investigate therapeutic antibiotic use in veterinary *and* human medicine. Further recommendations included a retraction of the previous endorsement of AGPs for calves, a rationalization of expert structures dealing with antibiotics, and turning salmonellosis into a notifiable disease.<sup>106</sup>

Reviewing therapeutic antibiotic use in human and veterinary medicine proved contentious: not only did it infringe on the legislative boundaries between the Ministries of Agriculture and Health, a new program of

105. Ibid., 3.

106. TNA MAF 287/450 (Annexe, ARC 22B/66, ARC & MRC. Joint Committee on Antibiotics in Animal Feeding. Second Report of the Scientific Subcommittee), 1–2.

<sup>104.</sup> TNA FD 1/8228 (Further observations on infective drug resistance in S. typhimurium Type 29), 1.

antibiotic reform also threatened to interfere with the MH's almost finalized new Medicines Act.<sup>107</sup> In view of the political situation, MH officials successfully pressed for a deletion of all references to human medicine during the main Netherthorpe Committee's final meeting in April 1966.<sup>108</sup> Submitted in early January 1967, the final report recommended merely a review of "the use of antibiotics in animal husbandry and veterinary medicine and its implications in the field of public health."<sup>109</sup> However, the scientific subcommittee's attached report stressed that evidence against subtherapeutic AGPs was inadequate.<sup>110</sup> In sum, the only area to be reviewed was veterinary antibiotic use.

The proposed review's limitation to veterinary medicine naturally irritated veterinarians. Complaining about the second Netherthorpe report's supposed anti-veterinary bias, the ARC blocked its publication in January 1967.<sup>111</sup> The mood in MAFF was more nuanced: while one official downplayed the report as an uncomfortable "storm in a teacup,"<sup>112</sup> others anticipated "a first-class row with the Royal [Veterinary] College and the BVA."<sup>113</sup> However, MAFF officials agreed that the ARC's decision to withhold the report's publication was unwise.<sup>114</sup> Powerless to override the ARC, MAFF officials lobbied the MH to extend the review to both agricultural and medical aspects of antibiotic use.

In doing so, officials cited a separate review of agricultural antibiotics by MAFF's Scientific Advisory Panel (SAP). Apparently anticipating an uncomfortable second Netherthorpe report, MAFF had commissioned the SAP with this review in 1965. Significantly, the SAP expert group on antibiotics was headed by Alastair Frazer, a food additives expert with close ties to the pharmaceutical industry.<sup>115</sup> Published in 1967, the SAP report denied the existence of imminent health threats resulting from agricultural antibiotic use. Regarding possible long-term dangers, the SAP recommended a national resistance study, a review of antibiotic control measures

107. Bud, Penicillin (n. 85), 181.

108. TNA MAF 287/450 (Minute, Macrae to Field, January 18, 1967), 2.

109. TNA MAF 287/450 (Annexe, ARC 2546/66, ARC & MRC. Joint Committee on Antibiotics in Animal Feeding), 1.

110. TNA MAF 287/450 (Annexe, ARC 22B/66, ARC & MRC. Joint Committee on Antibiotics in Animal Feeding. Second Report of the Scientific Subcommittee), 2.

111. TNA MAF 287/450 (Minute, Hensley to Bott, January 9, 1967).

112. TNA MAF 287/450 (Minute, Hensley to Bott, May 22, 1967).

113. TNA MAF 287/450 (Minute, Bott to Hensley, May 23, 1967).

114. TNA MAF 287/450 (Minute, Hensley to Bott, May 22, 1967).

115. D. W. Kent-Jones, "Obituary. Alastair Campbell Frazer," Proc. Soc. Analyt. Chem. 6 (1969): 209-10.

and more cooperation between medical and veterinary authorities.<sup>116</sup> Summing up the report, a MAFF official noted: "In other words, nothing we should do should impede the use of antibiotics in agriculture or food, though of course they must be used with reasonable safeguards."<sup>117</sup>

The ARC, MAFF, and the MH all stuck to their respective positions and the second Netherthorpe report remained unpublished. By July 1967, Minister of Agriculture Frederick Peart became involved. During a meeting with Frazer and senior MAFF officials, he agreed that the Netherthorpe report "created some unnecessary alarm, and that [it] picked out veterinarians."<sup>118</sup> Peart agreed to pressure the MH to extend the planned antibiotic review from veterinary to human medicine—thereby deflecting pressure from veterinarians.<sup>119</sup> In September 1967, the involved parties issued a joint press statement in which they publicized and accepted the second Netherthorpe report's recommendations regarding the simplification of advisory structures and the creation of a new antibiotic review committee.<sup>120</sup>

Issued nine months after the Netherthorpe report's original submission, the vague press statement reassured nobody. In the *New Scientist*, Anderson's friend Bernard Dixon attacked "the irritating British habit of seeking expert guidance on a technical matter and then pigeon-holing the advice when it comes."<sup>121</sup> Citing Anderson's work on infectious resistance, Dixon also referred to the dangers of multiresistant *E. coli* strains causing neonatal diarrhea in babies.<sup>122</sup> Two months later, Dixon's warnings sounded tragically prophetic. Described by Robert Bud in chilling detail, a resistant *E. coli* strain caused a severe outbreak of gastroenteritis among infants in the northeastern town of Middlesbrough. Poor hospital hygiene and transferring infected infants to other hospitals spread the infection. Fifteen infants died.<sup>123</sup>

The so-called Teesside deaths created a potent alliance for antibiotic reform between medical experts, animal welfare activists, environmental-

116. TNA MAF 287/450 (Minute, Wilcox to Hensley, Jan 9, 1967); TNA MAF 284/282 (SAP report, enclosed in: Minute, Bott to Parker, July 13, 1967), 12.

117. TNA MAF 284/282 (Minute, Bott to Parker, July 13, 1967).

118. TNA MAF 287/450 (Minute, Dickinson to Hensley, July 24, 1967).

119. Ibid.

120. TNA MAF 284/282 (Press Notice, 1 September 1967).

121. Bernhard Dixon, "Antibiotics on the Farm—Major Threat to Human Health," *New Scientist*, October 5, 1967, 33.

122. Ibid., 34.

123. Bud, *Penicillin* (n. 85), 178–81; House of Commons Debate, "Gastro-Enteritis (Tees-Side)," 762 (April 11, 1968), cc1619–30.

ists, and concerned consumers.<sup>124</sup> Caught in a whirlwind of public attention, officials knew that further regulatory delays were no longer feasible: minutes exchanged between MAFF and the MH reveal that concern first arose when the BBC's *Twenty-Four Hours* linked infant fatalities to antibiotic overuse in agriculture.<sup>125</sup> Previously postponed by an outbreak of footand-mouth disease, a meeting between agricultural and health officials was hastily scheduled for February 13, 1968. Because it was clear that one side would have to yield regarding the new review's terms of reference, the meeting was characterized by icy power plays between both ministries. In the end, the MH was able to block demands for an holistic antibiotic review: human medicine was the sole concern of the MH and MAFF had indirectly "accepted" the second Netherthorpe report's agricultural focus in the joint press statement.<sup>126</sup> Reporting on the meeting, MAFF officials complained that the MH had treated the new review's terms of reference as "a sacred cow which would not be sacrificed at any cost."<sup>127</sup>

The next difficult question to settle was the new review's membership. Feeling that the Netherthorpe Committee had been "over-weighted scientifically on the medical and para medical sides,"<sup>128</sup> MAFF was keen to shift the balance of power in the new antibiotics committee. Another point of contention was E. S. Anderson's role. Should he be a committee member, or should he function as an adviser? Both ministries were aware of Anderson's public influence but wary of his vocal support of antibiotic restriction and temperamental character. In order to control Anderson, the MH suggested co-nominating PHLS director James Howie.<sup>129</sup> Anderson himself saved officials from further headaches: eager to be nominated, he announced that he would refuse to give evidence if he were not appointed to the committee in April 1968.<sup>130</sup>

124. Kirchhelle, "Pyrrhic Progress" (n. 19), 105.

125. TNA MAF 287/450 (Minute, Wilcox to Hensley, December 22, 1967; Minute, Hensley to Williamson, December 29, 1967); Anderson claimed that the Teesside strains might have human or animal origins; TNA MAF 287/450 (Minute, Williamson to Hensley, January 25, 1968).

126. TNA MAF 287/450 (Minute, Parker to Bott, Field, Macrae, February 1, 1968); TNA MAF 287/450 (Note of Meeting "To Discuss the Second Report of the Joint ARC/MRC Committee," February 13, 1968).

127. TNA MAF 287/450 (Minute, Macrae, Inter-Departmental Meeting on the Nether-thorpe Committee Report, February 19, 1968).

129. TNA MAF 287/450 (Minute, G. J. L. Avery, Joint Committee on Antibiotics, April 25, 1968).

130. TNA MAF 287/450 (Minute, Tame to Secretary, April 29, 1968).

<sup>128.</sup> Ibid.

This attempt to pressure his way into official decision making was bound to backfire. His public partisanship made Anderson anathema to Britain's confidential system of corporatist consultation, which depended on experts' unanimous endorsement of resulting compromises. Already skeptical of Anderson, MAFF was now able to argue that he would endanger the public standing of the new review and its findings: "If the committee's conclusions were in line with Dr. Anderson's views, there would be the charge that we had biased it with prejudiced members; if it went the other way, Dr. Anderson would no doubt issue a minority report."<sup>131</sup> Even James Howie, who had previously refused to accept a committee position without Anderson's co-nomination, now changed his mind. A minute exchanged between MAFF and the MH noted triumphantly: "Dr. Howie has become impatient of the Prima Donna approach of his colleague Dr. Anderson and is no longer prepared to support him."<sup>132</sup>

By May 1968, all important decisions had been made: Anderson had been substituted with another public health expert, and molecular biologist and University of Edinburgh vice-chancellor Michael Swann had accepted chairmanship of the committee. Fearing public attacks by Anderson, MAFF had, however, withdrawn its nomination of Alastair Frazer. In a smart move, agricultural officials convinced the MH to nominate two veterinarians in Frazer's stead. Comprising two agriculturalists, three veterinarians, and two medical scientists, the new committee was weighted slightly in favor of agricultural interests.<sup>133</sup> Elated that the so-called Swann Committee could start its work, one official noted: "I must confess that there is no adequate reason for the fact that it took us some nine months . . . to set up a Committee to go further into the matter."<sup>134</sup>

Starting its work in July 1968, the Joint Committee on the Use of Antibiotics in Animal Husbandry and Veterinary Medicine had to strike a new compromise between agricultural, veterinary, medical, and public concerns. It also had to reconcile its proposals with the 1968 Medicines Act. In light of public interest, maintaining the status quo ante and requesting further reviews were not viable options. Pressure for decisive action further

131. TNA MAF 287/450 (Avery to Tame, May 2, 1968).

132. TNA MAF 287/450 (Minute, Carnochan to Tame, May 3, 1968); Anderson subsequently unsuccessfully approached MP David Kerr to lobby for his nomination to the committee; TNA MAF 287/450 (David Kerr [MP] to Rt. Hon. Cledwyn Hughes [MAFF], May 22, 1968).

133. TNA MAF 287/450 (Committee on the Use of Antibiotics in Animal Husbandry and Veterinary Medicine. Proposed Members).

134. TNA MAF 287/450 (Minute, Tame to Williamson, May 6, 1968).

increased between December 1968 and April 1969. In a bitter repetition of the Tees-side outbreak, thirty babies died of resistant gastroenteritis in two Manchester hospitals.<sup>135</sup>

Submitted in November 1969, the Swann report clearly acknowledged that agricultural antibiotic use contributed to resistance proliferation and had "caused some difficulties in veterinary practice and ha[d] caused harm to human health."<sup>136</sup> The transfer of resistance en bloc increased the likelihood of a "massive and rapid propagation of antibiotic resistant organisms"<sup>137</sup> as had already happened in the case of *S. typhimurium* Type 29. Although it claimed that horizontal resistance transfer was only a problem in enterobacteriacae, the report refused to accept that twenty years of use had proven agricultural antibiotics harmless. Despite its inability to quantify the hazard posed by agricultural resistance selection, the report stated that there was sufficient evidence to take action without allowing the "cry for more research" to "hold up implementation of our recommendations."<sup>138</sup>

The resulting recommendations were mostly extensions of the 1962 Netherthorpe report. The Swann report advised the government to cut the number of advisory bodies and install a permanent committee on all aspects of antibiotic use. It also called for a ban of antibiotic advertising to laypersons and further research. Answering contemporary veterinary activism, the report advocated the funding of preventive veterinary epidemiology at universities.<sup>139</sup> However, most significantly, the Swann report recommended extending the distinction between therapeutically useful and not useful antibiotics to already licensed AGPs. Antibiotics should be used as growth promoters only if they were of economic value, had little or no application as therapeutic agents, and did not impair the efficacy of therapeutic antibiotics. This latter recommendation also targeted scenarios in which resistance to AGPs was "part of a multiple resistance pattern transferable *en bloc.*"<sup>140</sup>

In concrete terms, the Swann report advocated a ban of penicillin and tetracycline-based AGPs. It also advocated assigning prescription-only status to the still unscheduled macrolide tylosin because of cross-resistance to erythromycin. Freely available sulphonamide and nitrofuran feeds should

<sup>135. &</sup>quot;Action Sought on Antibiotics after Babies' Deaths," *Times*, April 14, 1969, 2; "Baby-Killer Bug Traced," *Observer*, April 13, 1969, 7.

<sup>136.</sup> Report: Joint Committee on the Use of Antibiotics (n. 42), 40.

<sup>137.</sup> Ibid.

<sup>138.</sup> Ibid.

<sup>139.</sup> Woods, "Is Prevention Better Than Cure?" (n. 7), 113.

<sup>140.</sup> Report: Joint Committee on the Use of Antibiotics (n. 42), 45.

also be restricted due to their selection for multiple-resistant organisms. The availability of nontherapeutic AGPs like bambermycin, virginiamycin, and zinc bacitracin meant that the proposed restrictions would not cause economic harm.<sup>141</sup> Taken by itself, the first part of the Swann report marked a milestone in the history of precautionary substance regulation that was based on the strong likelihood—but not definitive evidence—of harm.

However, when it came to addressing antibiotic use beyond AGPs, the Swann recommendations were far less ambitious. The report attacked veterinary attempts to control salmonellosis with antibiotics and found it "hard to find any excuse in logic or theory" for the "prophylactic treatment of farm animals in the absence of infection."142 It also criticized antibiotic prescriptions for conditions like liver abscesses in cattle that could be remedied by changing husbandry practices. Concerned about rising chloramphenicol use, the report noted that a prescription ban would cause "little or no hardship to some veterinary practitioners, or their clients."143 However, in contrast to its at times scathing rhetoric, the report did not recommend enforceable reforms of veterinary antibiotic use or chloramphenicol bans. Despite noting that prescription rights were not "sacrosanct," it emphasized "that the veterinary surgeon and practitioner, like his medical counterparty, treasures the freedom . . . to prescribe as he thinks best in the interest of his patient."144 It was clear that this laissez-faire attitude had been controversial within the Swann committee. The report warned veterinarians to "temper credulity with a more critical analysis of the advantages and disadvantages of the antibiotics they prescribe."145 Remarkably, the report also noted that its chloramphenicol "decision may prove to have been mistaken."146

So why did the Swann committee restrict low-dosed therapeutic AGPs but leave higher-dosed prescriptions of the same drugs untouched? The answer lies in Britain's corporatist system. The carefully staffed committee had attempted to find an acceptable compromise between demands for absolute safety and unrestricted antibiotic access. The emerging compromise was an extension of the 1962 Netherthorpe recommendations and so finely balanced that it posed no challenge to any of the involved

141. Ibid., 46.
142. Ibid., 34, 52.
143. Ibid., 56.
144. Ibid., 49.
145. Ibid., 56.
146. Ibid.

parties. Preexisting conflicts with the MH had been solved by the 1968 Medicines Act, which had replaced "gentleman's agreements" with manufacturers' statutory obligation to apply to the new Veterinary Products Committee (VPC) and the Committee on Safety of Medicines (CSM) for product licenses.<sup>147</sup> More significantly, the Swann report's partial AGP ban managed to square the circle by addressing some of critics' concerns while leaving antibiotic-dependent husbandry systems unharmed. Farmers and animal nutritionists could either switch to nontherapeutic AGPs or ask veterinarians, who earned a 50 percent markup charge, for higher-dosed prescriptions. What happened with such prescriptions was up to the farmer.<sup>148</sup> In the face of contemporary R-factor knowledge, it was questionable whether extending measures designed to contain vertical resistance by differentiating between drug dosages and classes would curb horizontal resistance transfer.

However, in late 1969, widespread endorsement of the report and an upcoming election meant that Minister of Agriculture Cledwyn Hughes quickly committed his ministry to implement the Swann recommendations.<sup>149</sup> Coming into effect in 1971, the British ban on therapeutic AGPs ended an era of laissez-faire antibiotic regulation. Preframed during the early 1960s, the Swann report's corporatist compromise served as a model for nearly identical regulations passed by the European Economic Community (EEC) in late 1970.<sup>150</sup> The report's distinction between unsafe low-dosed uses of therapeutically relevant and safe low-dosed uses of supposedly irrelevant antibiotics institutionalized boundary values that would shape European antibiotic regulation until the 2000s.

#### Swann Song? Antibiotic Policy after 1969

The Swann report's long-term regulatory impact is all the more remarkable because it soon became apparent that partial antibiotic bans were not working. Ten years after Swann, contemporaries drew a bleak con-

147. TNA MAF 284/281 (Control of Antibiotics, February 1969), 1; TNA MAF 461/34 (Note of Meeting on the Future of the Joint Sub-Committee on Antimicrobial Substances, September 28, 1979), 1–2.

148. G. Armstrong, "Closed Shop Drugs?," *Farmers Weekly*, December 5, 1969, 49; Leonard Amey, "A Week of Many Moves," *Times*, November 24, 1969, 18.

149. Anthony Tucker, "Antibiotics to Be Banned from Animal Feeds," *Guardian*, November 21, 1969, 20; Leonard Amey, "Three Antibiotics Banned from Animal Food," *Times*, November 21, 1969, 2; "Rations, Drugs and Costs," *Farmers Weekly*, December 5, 1969, 102.

150. EEC Directive 70/524/EEC.

clusion. Despite Britain's 1971 ban of penicillin and tetracycline AGPs, agricultural antibiotic consumption had grown. Meanwhile, increased prescriptions of therapeutic antibiotics, cross-resistance, and changing categories of medical relevance meant that bacterial resistance to therapeutically relevant antibiotics was also rising.<sup>151</sup> With public interest dissipating and former critics wary of undermining the original compromise on antibiotic bans,<sup>152</sup> the Swann report's fate highlights the downsides of corporatist decision making.

Problems were further exacerbated by the watering down of important Swann recommendations, which might have redressed the situation. Established after prolonged negotiations in 1973, the Joint Sub-Committee on Antimicrobial Substances (JSC) received neither funds nor power. As a subcommittee of the VPC and CSM, it was soon demoted to processing VPC licensing requests. After only six years, disgruntled members announced that they would dissolve the committee if they did not receive new terms of reference.<sup>153</sup> Unwilling to devolve any power or funds, its parent committees agreed to disband the JSC in the early 1980s.<sup>154</sup>

Bowing to protectionist demands, a limited monitoring program for antibiotic resistant organisms in meat imports had been established in 1970.<sup>155</sup> Initial results were to be evaluated by an interdepartmental committee and conducted by E. S. Anderson, who—with characteristic bluntness—had already derided it as "eyewash."<sup>156</sup> However, because of EEC membership negotiations, Britain's program of "spreading the Swann gospel"<sup>157</sup> via import monitoring was soon put on hold.<sup>158</sup> Arguing that Britain should put its "own house in order"<sup>159</sup> first, officials anticipated that new

151. R. Braude, "Antibiotics in Animal Feeds in Great Britain," J. Animal Sci. 46 (1978): 1425–36, quotation on 1429–31; John Harvey and Liz Mason, The Use and Misuse of Antibiotics in UK Agriculture. Part 1: Current Usage (Bristol: Soil Association, 1998), 10.

152. Herbert Williams Smith, "Why Has Swann Failed?," Brit. Med. J. 280, no. 6230 (1980): 1537.

153. TNA MAF 461/34 (James Howie to Chairmen of CSM and VPC, August 7, 1979), 1–2.

154. TNA MAF 461/34 (Note of Meeting on the Future of the JSC on Antimicrobial Substances, September 28, 1979), 1–4.

155. TNA MAF 416/85 (Minute, Blake, August 27, 1970).

156. TNA MAF 416/85 (Minute, Carnochan, April 30, 1970).

157. TNA MAF 416/85 (Minute, Doling, September 1, 1970).

158. TNA MAF 416/85 (Minute, Doling, November 18, 1970), 1-2.

159. TNA MAF 416/85 (Minute, Stoker, June 16, 1971).

EEC, Irish, and Danish antibiotic bans would make import monitoring superfluous.<sup>160</sup> After two years of debates, plans to monitor both imported and home-produced meat for resistant bacteria were quietly dropped.

The stagnation of resistance monitoring was not limited just to meat. Since the 1960s, experts had called for an extension of routine resistance surveillance to *E. coli*.<sup>161</sup> In the wake of a Mexican typhoid outbreak with transferable chloramphenicol resistance, PHLS researchers were particularly alarmed when they found widespread plasmid-mediated chloramphenicol resistance in random samples of British *E. coli*.<sup>162</sup> However, with PHLS finances undergoing a series of critical reviews from the mid-1970s onward,<sup>163</sup> no expansion of routine surveillance to *E. coli* occurred.

Attempts to monitor meat for antibiotic residues initially also stagnated. As Anne Hardy has shown, Britain's meat inspection infrastructure was relatively weak and did not have the resources and powers necessary for systematic residue controls.<sup>164</sup> Following Britain's EEC accession in 1973, Directive 64/433/EEC initially permitted the coexistence of differing national rules and food monitoring systems.<sup>165</sup> However, during the mid-1970s the EEC attempted to harmonize monitoring requirements and several export consignments of British meat were rejected because of antibiotic residues.<sup>166</sup> Although it managed to water down German-inspired EEC monitoring plans in 1978,<sup>167</sup> Britain grudgingly established a very limited national meat monitoring program in 1981.<sup>168</sup>

160. TNA MAF 416/85 (Minute, Doling, April 24, 1970), 4.

161. TNA FD 1/8228 (ARC/MRC Joint Committee on Antibiotics in Animal Feeding. Scientific Subcommittee June 22, 1965), 3.

162. TNA MAF 386/46 (Minutes 24th Meeting PHLS/AHD Advisory Committee, July 24, 1974), 4.

163. TNA MH 154/1315.

164. Anne Hardy, "John Bull's Beef: Meat Hygiene and Veterinary Public Health in England in the Twentieth Century," *Rev. Agric. Environ. Stud.* 91, no. 4 (2010): 369–92, quotation on 369.

165. TNA MAF 461/67 (J. A. Davies to J. E. Tugwell, November 16, 1977), 1.

166. TNA MAF 461/67 (Steering Group on Food Surveillance Sub-Group on Antibiotic Residues in Food, 1st Meeting, April 20, 1976), 5, 7.

167. TNA MAF 461/68 (EEC, Summary Report of Meeting with Representatives of Community Institutions or Member Governments, Working Party "Veterinary Legislation" Sub-Group "Residues" [May 25–26, 1978], Draft Directives on Undesirable Residues in Fresh Meat, May 30, 1978), 1–4.

168. TNA MAF 461/70 (Working Party on Veterinary Residues in Meat and Meat Products, National Meat Monitoring Programme Year 1 Results, October 13, 1982). Over a decade after Swann, Britain had no reliable monitoring system for antibiotic residues or bacterial resistance beyond the PHLS's routine surveillance of *Salmonella*. Without reliable data on environmental resistance and R-factors, it was difficult to argue for systematic reforms of antibiotic use. Although officials continued to praise it, Britain's Swann doctrine remained only half implemented and its boundary values for "safe" agricultural antibiotic use appeared increasingly dubious. Elected in 1979, the Thatcher government's philosophy of minimum government did not bode well for antibiotic reform either. Over the next seventeen years, Britain devoted itself not to antibiotic regulation but to blocking further reform proposals.<sup>169</sup>

Meanwhile, the mid-1980s saw Scandinavian states and later the European Union (EU) turn into a new force for antibiotic reform. Attempting to restore trust in British agriculture following the 1996 "mad cow disease" crisis, the New Labour government supported the EU's 1997 ban of avoparcin feeds for pigs and poultry and bans of four further AGPs in 1998. Significantly, Britain also agreed to support the establishment of systematized European monitoring of antibiotic resistance in sentinel organisms. In 2001, antibiotic residue monitoring was also updated with the installation of an independent Veterinary Residues Committee. National monitoring programs had to be approved by the EU on an annual basis. When the EU decided to ban all antibiotic growth promotion by 2006, the 2003 vote was supported by the United Kingdom.<sup>170</sup>

#### Conclusion

This paper has tracked British antibiotic regulation from antibiotics' 1950s mass introduction to agriculture to the pioneering 1969 Swann report and its subsequent fate. It has highlighted that antibiotics were introduced to British agriculture despite warnings about their risks and the inadequacy of existing regulatory infrastructure. Following 1953, laissez-faire drug regulation, a lack of basic monitoring, blurred responsibilities, and notions of vertical resistance proliferation allowed nonhuman antibiotic use to flourish. Within a decade, antibiotics had begun to form what

170. Kirchhelle, "Pyrrhic Progress" (n. 19), 161-66, 212-19.

<sup>169.</sup> Richard Young et al., The Use and Misuse of Antibiotics in UK Agriculture. Part 2: Antibiotic Resistance and Human Health (Bristol: Soil Association, 1999), 42.

Clare Chandler, Eleanor Hutchinson, and Coll Hutchison have termed an infrastructure for the rapid expansion of Britain's livestock sector.<sup>171</sup>

Meanwhile, enterprising scientists like Herbert Williams Smith and Ephraim Saul Anderson used PHLS phage-typing to highlight the threat posed by agricultural resistance selection. Around 1960, these warnings triggered the first resistance-focused review of agricultural antibiotic use. However, professional power struggles and the corporatist nature of British advisory committees led to a technical "fix" of agricultural antibiotic use. Drawing on notions of vertical resistance transfer, the 1962 Netherthorpe report created a new set of boundary values by calling for antibiotic licensing to distinguish between valuable therapeutic antibiotics, which should be reserved for humans, and less valuable nontherapeutic antibiotics, which could be fed to animals. The Netherthorpe compromise prefigured over three decades of antibiotic regulation and promised to satisfy farmers' demands for ongoing antibiotic access and veterinary and medical demands for greater antibiotic control.

However, within three years, E. S. Anderson's publications on horizontal resistance proliferation severely undermined the 1962 compromise. Formerly viewed as a localized phenomenon, antibiotic resistance on farms turned into an environmental risk. Anderson's research on *S. typhimurium* Type 29 and a new environmental understanding of "infectious resistance" challenged not only AGP use but also aspects of medical and veterinary antibiotic use. What followed was a lengthy series of corporatist power struggles over antibiotic access behind closed doors.

In 1969, the resulting Swann report promised a lasting reform of agricultural antibiotic use by banning therapeutic AGPs and was one of the first examples of precautionary European risk regulation. However, a closer examination reveals that instead of rethinking antibiotic policy from the perspective of "infectious resistance," the Swann committee attempted to contain horizontal resistance transfer within an already established policy matrix. Despite its powerful rhetoric and acknowledgment of Anderson's research, the report was mostly an extension of the 1962 Netherthorpe compromise. Aiming to satisfy all parties within the corporatist decision-making framework, the report's recommendations made little difference on farms and even less difference for bacteria. While the Swann gospel turned into a successful British export, agricultural

<sup>171.</sup> Clare I. R. Chandler, Eleanor Hutchinson, and Coll Hutchinson, *Addressing Antimicrobial Resistance through Social Theory: An Anthropologically Oriented Report* (London: LSHTM, 2016), 16–17.

and veterinary antibiotic use and bacterial resistance continued to rise. Meanwhile, the watering down of resistance monitoring programs and critics' fear of jeopardizing the original compromise allowed the Swann report to ossify into a doctrine.

What originated as a British corporatist solution to contain vertical resistance also proved remarkably enduring at the international level.<sup>172</sup> Despite marking an important step, the EU's 2006 AGP-ban can be interpreted as the fulfilment of a regulatory trajectory dating back to differentiations between safe and unsafe antibiotic use of the 1960s. Although systematic EU-wide resistance monitoring has repeatedly challenged antibiotic overuse, current EU regulations continue to follow the 1962 Netherthorpe report's logic: lay access to low-dosed antibiotics is restricted while higher-dosed antibiotic use via veterinary prescriptions mostly evades regulatory scrutiny. The post-2006 situation bears further resemblances to the post-Swann situation: inter-European responsibilities are diffuse, pharmaceutical and veterinary interests remain strong, and the temptation is great to rest on the laurels of the 2006 ban. Meanwhile, European intensive agriculture remains antibiotic dependent. Despite recent reductions of domestic agricultural antibiotic use, British farm and companion animals received approximately 337 tons of antibiotics in 2016-this still marks a significant increase from the 168 tons of consumption estimated by the Swann Report almost 50 years ago for 1967.<sup>173</sup> Despite cyclical waves of criticism dating back to the late 1950s, a holistic antibiotic policy has yet to emerge in the EU or elsewhere.

Meanwhile, official memories are short. The history of agricultural antibiotic use shows how important it is for historians to engage decision makers and highlight recurring blind spots and path dependencies of public health regulation. Although it would be presumptuous to offer ready-made solutions for an extremely complex problem, it seems obvious that a critical reassessment of our entire antibiotic infrastructure is necessary to halt the Swann song of bacterial resistance.

172. U.S. FDA regulators futilely pressed for Swann inspired from the 1970s onwards, Kirchhelle, "Pyrrhic Progress" (n. 19), 275–320.

173. Veterinary Medicines Directorate, UK Veterinary Antibiotic Resistance and Sales Surveillance Report (New Haw: VMD, 2017), 20; Report: Joint Committee on the Use of Antibiotics (n. 42), 65.

\*

CLAAS KIRCHHELLE is research associate at the University of Oxford's History Faculty and the Oxford Martin School. He is also Junior Research Fellow at Wolfson College. He specializes on the global history of antibiotic use, resistance, and regulation. His dissertation, "Pyrrhic Progress: Antibiotics and Western Food Production (1949–2015)," won the University of Oxford's 2016 Dev Family Prize for the best dissertation in history of medicine and is forthcoming with Rutgers University Press. He is currently researching the history of bacteriophage typing and Britain's Public Health Laboratory Service (PHLS).