
Index

- Abbott Laboratories, in CMR synthesis program, 92
- Abraham, Edward P.
and beta-lactam ring, 113-114
and cephalosporins, 127, 207
in early penicillin research, 3, 28, 33
on Florey's trip, 52
oxazolone-thiazolidine structure proposed by, 102
penicillin analysis by, 94, 95, 96, 98
and penicillin inactivation, 131
also 53
- Acylation, in penicillin synthesis, 160, 172, 175, 177, 178, 179, 184. *See also* 6-APA
- Adams, Roger, 88, 89, 90
- Adkins, Homer, 112-113
- Adrian, E. D., 53
- Alicino, Joseph F., 97
- Allergenicity, reducing, 133-134, 208
- American Chemical Society Award in Pure Chemistry, to Sheehan, 126
- American Cyanamid, in CMR synthesis program, 92
- Alston, Dr. Aaron, 35
- Amidase, penicillin inactivation by, 132, 133
- Ampicillin, and Gram-negative microorganisms, 131
- Analysis. *See* Penicillin, chemical analysis of
- Anchel, Marjorie, 90
- Atomic Energy Commission, 126
- Azlactone-thiazolidine structure. *See* Oxazolone-thiazolidine structure
- Azo compounds, 37-39
- Prontosil, 38
- Bachmann, Werner, 8, 91, 92, 106, 118
- Baker, Wilson, 94, 95, 102, 114
- Ballard, Steve, 106
- Baxter, James Phinney, 49
- Bayer Co., 58
- Beecham Inc. laboratories
alleged patent fraud by, 193-196
and Bristol Laboratories, 169, 175-176
and para-aminopenicillin G, 170
patent claims by, 173, 178, 179-180, 183-188, 192-197
and patent claim tests, 186, 188-192
patent motives of, 197
products of, 169-170
replication of Sheehan synthesis attempted by, 185, 187, 192-193, 194-195
- 6-APA production by, 126-127, 160, 169, 172-173, 179
- Benson, A. J., 69, 70
- Benzylpenicillin. *See* Penicillin, types of, penicillin G
- Beta-lactam ring (beta-lactam structure), 6-7, 198. *See also* 6-APA
- anti-penicillinase protection for, 132-133
and carbodiimides, 142, 153, 156
- Ernst Chain favoring of, 29
and difficulty of penicillin synthesis, 6-7, 9, 167
and hydroxylamine test, 170-171
importance of, 127, 207, 208

- in Sheehan's penicillin synthesis, 15, 152–157, 159
Beta-lactam thiazolidine structure, 104. *See also* 6-APA
controversial discovery of, 113–115
demonstration of, 110–113
proposed for penicillin, 103–104
Robinson opposition to, 29, 114, 115
Beth Israel Hospital, research at, 5
Bickel, Lennard, 57, 58, 63
Big Three. *See* Merck & Company; Pfizer Inc.; Squibb, E. R., and Sons
Blocking groups
definition of, 154
in Sheehan's synthesis, 153, 154–157
Board of Patent Interferences,
Sheehan-Beecham decision by, 196–197
Bok, Derek, and DNA issue, 204
Bose, Ajay, 145–146, 150, 188, 190, 191, 192
Bowman, Philip, 174
Bristol Laboratories
and Beecham, 169, 175–176
as patent licensee, 173–174
and penicillin for industrial use, 76
in penicillin production, 160
and Sheehan, 128–129, 150, 169, 175–176, 177
and 6-APA, 168, 169
British Journal of Experimental Pathology, Florey as editor of, 30
British Medical Journal, and Oxford interpretation of penicillin discovery, 19, 25–26
British Medical Research Council, 56, 63, 81, 165
Bunday, Harvey H., 54
Burn, J. H., 66, 97
Bush, Vannevar
and CMR programs, 46, 74, 86, 87–88, 92, 202
and Merck, 83
and OSRD, 45
and patents, 77, 162
and pharmaceutical industry, 49–50
also 72, 75, 76
Business. *See* Pharmaceutical industry
Butenandt, Adolf, 125
B vitamins, and penicillin-synthesis rationale, 82
Carbodiimides, 137–145, 146–149. *See also* DCC
and beta-lactam ring, 142, 153, 156
in penicillin synthesis, 149, 153, 156, 158, 159
and peptide bonds, 137–141, 142–143, 144–145
Carbon dioxide, in analysis of penicillin, 101, 102
Carboxylic acid, in penicillin analysis, 101, 102
Carroll, 190, 191
Carter, H. E., 91, 92, 109
Censorship. *See* Security regulation
Censorship Committee, CMR, 56
Cephalosporin C
and beta-lactam ring, 127
and Gram-negative microorganisms, 131
Chain, Ernst
background of, 28
and Beecham, 170, 175
and beta-lactam ring, 114, 115
on commercial possibilities, 164–165
early penicillin research by, 3, 19, 20, 30, 33
on Fleming's contribution, 20
and Florey-Heatley trip, 64
Nobel Prize to, 18, 27–28
oxazolone-thiazolidine structure
proposed by, 102
and penicillamine, 97
penicillin analysis by, 94, 95, 96, 98
on penicillin synthesis, 80, 160
reputation of, 27
and Sir Robert Robinson, 29
also 113, 176
Chemical analysis. *See* Penicillin, chemical analysis of

- The Chemistry of Penicillin* (Woodward), 122, 200
- Chemotherapy
history of, 36–39
low success ratio in, 39
and penicillin research, 26, 39
pessimism over, 26–27
- Cheney, Lee, 160, 175
- Churchill, E. D., 41
- Churchill, Winston, treatment of, 61
- CIBA Pharmaceutical Co., 57
- CIBA Symposium, Sheehan
remarks on 6-APA at, 179
- Clark, William, 72
- Clarke, Hans
and CMR programs, 89, 90, 122
and Sheehan patent case, 181, 204
and thiazolidines, 99, 100
also 106, 107, 109
- Clayton, John Peter, 185, 193,
194, 195–196
- Clowes, G. H. A., 72
- Clutterbuck, Percival W., 19, 26,
30, 94, 98, 99
- CMR. *See* Committee on Medical
Research
- Cocoanut Grove fire, as penicillin
trial, 40–43
- Coghill, Robert D.
and CMR programs, 48, 56, 73,
74, 89, 92
and Florey-Heatley trip, 66
penicillin analysis by, 106
also 51, 87, 96
- Colebrook, Leonard, 39, 62
- Collagen, in Sheehan research,
146–147
- Columbia Medical College, re-
search at, 5
- Commercial Solvents, “admission
ticket” of, 75
- Committee on Medical Research
(CMR), Office of Scientific Re-
search and Development, 4,
45–51
in Cocoanut Grove fire, 40–42
funding of, 45–46
membership of, 45
- Microbial Therapeutics confer-
ence of, 69–71
- and patent rights, 49–50, 72,
75–76, 77, 92, 162, 202
- and penicillin research, 4, 47–51,
68–71, 199
- and penicillin synthesis, 4, 49, 81,
87–92, 116, 121–122, 161
- and pharmaceutical industry,
49–50, 69–75, 201–202
- production/synthesis decision by,
49
- security measures by, 54–56
- Competition, commercial, 73, 202.
See also Pharmaceutical indus-
try, and patent rights
- “Compound VIII,” in Sheehan
synthesis, 154
- Constitution, U.S., on patents, 161
- Controversies
Anglo-American, 4–5, 63, 162,
197
over discovery, 18–20, 25–26,
27–28, 113–115, 198
- Cope, Arthur, 128, 150
- Corey, E. J., 150
- Corn steep liquor, in penicillin
production, 67–68
- Cortisone, and Lewis Sarrett, 12
- Counter-current extraction
method
of Craig, 118, 120–121
of Podbieliak, 85–86
- Coupling agents, 149, 200. *See also*
Carbodiimides
- Court cases. *See* Patent rights;
Sheehan, John C., patent
rights of
- Craig, Lyman C., 118, 120
- Cram, Donald, 86
- Cruikshank, Philip A., 150, 151
- Cutter Laboratories. “admission
ticket” of, 75
- Cyclonite (RDX), Sheehan’s work
on, 8
- Dale, Sir Henry, 53, 56, 63, 77
- Dawson, Martin Henry, 35
- DCC (dicyclohexylcarbodiimide).
See also Carbodiimides
importance of, 141
and peptide bonds, 138–141,
142–143, 144–145

- preparation of, 138
in Sheehan's penicillin synthesis, 153, 158, 159
Deep fermentation
at Northern Regional Research Laboratories, 66
and U. S. manufacture of penicillin, 52
and wartime security, 57
Degradation products, of penicillin, 101, 102
Demerec, M., 48
Desacylpenicilloic acid, structure of, 100
Desulfurization
in beta-lactam proof, 110–111
in biotin analysis, 118
Diisopropylcarbodiimide, and beta-lactam ring, 156. *See also* Carbodiimides
DNA
and patent protection, 205
and private profit, 203
Dochez, A. R., 45
Domagk, Gerhard, 37, 38, 39
Doyle
as Beecham representative, 160, 175
in patent actions, 178, 183, 185, 189, 193, 196
Dreyer, George, 30
Drinker, Cecil, 165
Drinker, Phillip, 165
Drug industry. *See* Pharmaceutical industry
Dutcher, J. D., 90
Dyes
and chemotherapy, 37–38
as duplication of nature, 93
and thiazoles, 100
Dyson Perrins laboratories, 29. *See also* Oxford University, penicillin research at
Ehrlich, Paul, 26, 36–37
“Enchanted ring,” 6, 199, 208. *See also* Beta-lactam ring
Epstein, L. A., 28
Espionage, international
CMR concern with, 57–58
U.S. World War II efforts in, 59
Falk, L. A., 28
Faxon, N. W., 41
Fermentation. *See Deep fermentation; Penicillin, biological production of*
Ferrebee, Joseph W., 164
Ferris, 188, 189, 190
Fischer, Hans, 58
Fleming, Sir Alexander
analytic work by, 94
in defense of research contribution, 26
on Gram-negative immunity, 130
on need for synthesis, 26, 84
Nobel Prize to, 18, 27–28
penicillin discovery by, 2, 3, 10, 19, 20–22, 23–26, 30
reputation of, 27
research contribution of, questioned, 19–20
training and previous career of, 22–23
Fletcher, Charles M., 32, 33
Floe, Carl F., 166
Florey, Sir Howard
claims by, 18–19
on commercial possibilities, 164–165
and corn steep liquor, 68
on Fleming's contribution, 20
fund-raising efforts of, 63–64
at Microbial Therapeutics conference, 69
on need for synthesis, 84
on need for U.S. manufacture of penicillin, 51–52
Nobel Prize to, 18, 27–28
on Northern Regional Research Laboratory, 74
and penicillamine, 97
in penicillin analysis, 95
penicillin research by, 3, 4, 5, 19, 20, 28, 29–35
reputation of, 27
and security regulations, 55, 57
U.S. connections of, 53
and U.S. penicillin development, 162
U.S. visit by, 5, 35, 43, 51, 64–66, 70

- Folkers, Karl
on Homer Adkins, 111–113
and CMR programs, 69
on desulfurization, 110, 117–118
at Merck, 83, 90
on Sir Robert Robertson, 105
streptomycin research of, 12, 13
synthesis of penicillin by, 118
on U.S.-British relationship, 162
on du Vigneaud work, 117
on R. W. Woodward, 107
also 50
- Food and Drug Administration, U.S., 126
- Forrester, Jay, 173
- Foster, Jackson, 83
- Frank, Victor, 155
- Fulton, John, 19–20, 43, 65
- Gelatin, Sheehan research on, 147
- Germany, World War II penicillin research efforts by, 57–59
- Goldsworthy, N. E., 30
- Gram, Hans Christian, 36
- Greenberg, Daniel S., 65
- Gross, Erhard, 141
- Guinea pigs, penicillin toxic to, 32
- Hair curling solutions, Sheehan research on, 148
- Hantzsch, A., 99
- Harris, Stan, 111, 118
- Harrison, Ross G., 36, 43, 65
- Harrop, George A., 90
- Harvard University, and DNA question, 203–204
- Hastings, A. Baird, 45, 75
- Heatley, Norman G.
and Holt extraction process, 94
at Microbial Therapeutics conference, 69
penicillin research by, 3, 28, 30–31
U.S. visit by, 35, 51, 64–68, 70
also 33
- Heatley-Moyer method of penicillin production, 67–68
- Heilman, Dorothy H., 35–36
- Henery-Logan, Ken, 150, 151, 152, 154, 176, 177, 190
- Herrell, Wallace E., 5, 35–36
- Herrick, H. T., 74
- Hess, George, 138–141, 144
- Hobby, Gladys, 35
- Hockenhull, 178, 180, 181, 182
- Hodgkin, Dorothy Crowfoot, 108, 109, 110, 111, 113, 114
- Hoffman, Klaus, 117
- Hoffman-LaRoche Inc., 57
- Holt, L. B., 94
- Hooper, Irving, 175
- Hoover, Herbert, on research funding, 64
- Hörlein, Heinrich, 37–38
- I. G. Farbenindustrie, 37, 58
- Immunotherapy, vs. chemotherapy, 27, 37
- Industrial espionage, and CMR secrecy, 57
- Industry. *See* Pharmaceutical industry
- Influenza, Fleming research on, 24
- Interference, patent
Beecham claim of, 178, 183–184
definition of, 178
Patent Office declaration of, 185–186
- Inter partes* tests, in patent case, 186, 188–192
- Jackson, Judge Joseph R., 181, 182, 204
- Jacobs, Albert L., Jr., 189, 190
- Japan, World War II research efforts by, 59–62
- Jefferson, Thomas, on patents, 161
- Jewett, Frank B., 76
- Johnson, David L., 150, 151
- Johnson & Johnson, and Sheehan suture research, 148–149
- Kato, 178, 181, 182
- Keefer, Chester, 19–20, 43, 73, 76, 202
- Kennerson, W. H., 109
- Keretczky, John, 117
- Killian, James R., Jr. 166
- Kirk, Norman T., 19, 84
- Klarer, Josef, 38

- Korean War, and penicillin production, 125
- Lancet*
- Florey reports in, 34–35
 - Oxford group report in, 20
- Laubach, Gerald D., 150
- Laughlin, Joseph M., 41
- Laurence, William, 81, 180
- Lazell, H. G., 175
- Lederle, and cooperative research efforts, 71, 72
- Legal issues. *See* Patent rights; Sheehan, John C., patent fights of
- Lein, Joseph, 160, 175
- Lengyel, Istvan, 145
- Leonard, Nelson, 125
- Levaditi, Claude, 5
- Li, C. H., 138
- Lilly, Eli, and Co.
- "admission ticket" of, 75
 - in CMR synthesis program, 92
- Little, Arthur D., as Sheehan/MIT representative, 174
- Long, Perrin H., 39, 48, 62
- Lovell, Reginald, 19, 26, 94, 98
- McKeen, John E., 125
- McLean, Boustead and Sayre (law firm), 180
- MacPhillamy, H. B., 90
- Mader, W. J., 86
- Magee, General James G., 54, 55
- Major, Randolph, 11, 12, 70, 83, 89, 112, 117
- Manhattan Project, compared with penicillin synthesis, 1, 203
- Massachusetts General Hospital, and Cocoanut Grove experiment, 41, 42
- Massachusetts Institute of Technology (MIT)
- patent-rights view of, 166
 - and Research Corporation, 173–174
- Sheehan at, 9, 14–15, 135, 145–146, 150–151, 166, 167
- and Sheehan patent claims, 166, 173. *See also* Sheehan, John C., patent applications of
- Sheehan's penicillin tested by, 177
- Matthiesen, C. H., Jr., 88
- Mayo Clinic, research at, 5
- Medical Research Council, Great Britain, 56, 63, 81, 165
- Meinhofer, Johannes, 141
- Mellanby, Sir Edward, 57, 63
- Melville, Donald B., 117
- Menotti, Amel, 128, 150, 160, 168, 169, 174, 175
- Merck, George, 75
- Merck & Company
- "admission ticket" of, 75
 - and Anglo-U.S. cooperation, 53
 - biological production by, 70
 - and B vitamins, 82
 - in "closed corporation," 73
 - in CMR synthesis program, 88, 89–90, 91, 92
 - and Cocoanut Grove disaster, 42
 - and cooperative research efforts, 71, 88
 - diligence of, 54
 - early penicillin involvement by, 69
 - and Florey, 53
 - and oxazolone-thiazolidine structure, 102, 103
 - and penicillamine, 205
 - and penicillin analysis, 95, 111
 - penicillin purification work by, 86
 - penicillin synthesis by, 115, 118, 126
 - penicillin synthesis incentives of, 81–82
 - pre-eminence of, 75, 82–83, 88, 201
 - research facilities of, 50–51
 - research group at, 11
 - and Lewis Sarrett, 12
 - and Sheehan after leaving, 135
 - Sheehan helped by, 129
 - Sheehan's work at, 8
 - and 6-APA production, 172
 - and du Vigneaud, 117
- Methicillin, and penicillinase resistance, 132
- Meyer, Karl, 35, 87, 96
- Microbial Therapeutics conference, 69–71 *See also* Committee on Medical Research

- Mietzsch, Fritz, 38
Morrell, Theodor, 58
Moses, Alvin, 177
Mote, John R., 53
Moyer, Andrew J., 67
Mozingo, Ralph, 90, 110, 111, 115
Mussey, R. D., 36
- National Academy of Science,
Committee on Chemo-
therapeutic and Other Agents,
62
- National Research Council, 20, 45
- National Type Collection
Laboratories, 57
- Nayler, J. H. C., 178, 193, 194,
195–196
- Nobel Prize
to Butenandt (1939), 125
to Chain, Fleming, Florey (1945),
18, 27–28
to Domagk (1938), 39
- Northern Regional Research Laboratory, U.S. Department of Agriculture, Peoria, Illinois, 66–68
- CMR support for, 48
and information exchange, 73, 74
penicillin production by, 67–68
- NRC. *See* National Research Council
- Nuffield Foundation, 63
- O'Brien, Dan, 43
- Occam, William of ("Occam's Razor"), 154
- Office of Scientific Research and Development (OSRD). *See also* Committee on Medical Research
establishment of, 44
function of, 44–45
and patent rights, 202
"Ordinary skill in the art," in patent case, 182, 185
- OSRD. *See* Office of Scientific Research and Development
- Oxacillins, and penicillinase resistance, 432
- Oxazolone, structure of, 119
- Oxazolone-thiazolidine structure, 103, 119
and penicillin, 9, 102–103, 104–106
plausibility of, 104
- Robinson's championing of, 29, 104–106, 108, 114, 115
- X-ray analysis of, 113
- Oxford group
and penicillamine, 54
penicillin research by, 3, 20,
28–30, 32, 115. *See also* Florey,
Sir Howard, penicillin research by
- Oxford interpretation, of discovery of penicillin, 18–19, 25–26
- Oxford unit (of penicillin quantity), 31
- Oxford University, penicillin research at, 3, 90, 95. *See also* Oxford group
- Paine, C. G., 30
- Para-aminopenicillin G, 170, 172, 175
- Parke, Davis & Co., in CMR synthesis claim, 178–181,
- Pasteur, Louis, 37
- Pasteur Institute, 57, 59
- Patent Office
interference declaration by, 185–186
pharmaceutical industry trust in, 201–202
and Sheehan's penicillin synthesis claim, 178–181, 185–186
- Patent rights. *See also* Interference, patent
Beecham applications for, 173, 178, 179
Beecham challenges against Sheehan, 179–180, 183–188, 192–197
Beecham, Sheehan petition against, 193–196
British government interest in, 167 and CMR, 49–50, 72, 75–76, 77, 92, 162, 202
criteria for, 162–163
and Drinker respirator precedent, 165–166, 203

- in fermentation process, 76
international, 77
Moyer claim to, 67
in penicillin synthesis, 76
in penicillin V vs. G, 76
and pharmaceutical industry,
 49–50, 72–73, 75–77, 204
postwar rush for, 72–73, 161–
 162
and principles of nature, 163, 164
in semisynthetic penicillins,
 76–77
Sheehan applications for, 166,
 169, 173–175, 176, 177–180
Sheehan-Beecham *inter partes*
 tests of, 186, 188–192
Sheehan legal battles for, xii–xiii,
 180–188, 192–197
and Steenbock irradiation case,
 163–164
Peck, R. L., 50, 69, 90
Penicillamine
 analysis aided by, 98
 and commercial applications, 76
 discovery of, 96–97
 as essential to penicillin, 99
 and Oxford group, 54
 in penicillin analysis, 102
 structure of, 101, 119
Penicillaminic acid, and penicillin
 analysis, 97
Penicillic acid, and penicillin
 synthesis, 119, 120
The Penicillia (Thom), 21
Penicillin
 accenting the word, xiii
 allergenicity of, 133–134, 208
 black market in, 78
 and Cocoanut Grove fire, 40–43
 counterfeit, 78
 discovery of, 2–3, 10, 19, 20–22,
 23–26, 30
 early shortage of, 42–43
 first clinical trials of, 32–34, 35
 and Gram-positive vs. Gram-
 negative, 130–131
 and industrial use, 76
 initial disregard of, 2–3
 microbe resistance to, 131–132,
 208
 worldwide spread of, 78
Penicillin, biological production of
 and CMR, 4, 49–50
 dependence on, 109
 difficulties in, 85
 Fleming's method of, 66–67
 Heatley-Moyer method of, 67–68
 at Northern Regional Research
 Laboratory, 67–68, 69
 and pharmaceutical industry, 49,
 50–51, 69–70, 75–76
 and pH level, 69–70
 and Podbielniak extractor, 85–86
 success of, 7
 and synthesis program, 80, 81,
 82, 86–88
Penicillin, chemical analysis of. *See also* Penicillin, synthesis of
 beta-lactam-thiazolidine structure
 proposed, 103–104
 beta-lactam-thiazolidine structure
 proven, 110–113
 compromise formulas proposed,
 106–107
 degradation products, 101, 102
 early formulas, 95, 96
 methods for, 96, 108, 110–111,
 122
 and molecular weight, 6, 95, 205
 more recent methods, 205–206
 oxazolone-thiazolidine structure
 proposed, 102–103, 104–106
 and penicillamine, 96–97, 99
 and penicilloic acid, 100–101
 sulfur discovered, 97–99
 and thiazolidines, 99–100
 and treatment problem, 95
 through X-ray crystallography,
 108–109, 111, 113
Penicillin, research on
 Anglo-American controversies
 over, 4–5, 63, 162, 197
 Anglo-American cooperation in,
 51, 52–56, 62, 63–68, 77
 and attitude toward
 chemotherapy, 26, 39
 blind spots in, 95, 103–104, 167,
 171
 and chemical modifications, 124
 through CMR, 4, 47–51, 69–71,
 199
 crystallization achieved, 87

- Penicillin, research on (cont.)
discovery controversies, 18–20,
25–26, 27–28, 113–115, 198
by Fleming, 10, 19, 20–22,
23–26, 30
by Florey et al. (Oxford group),
3, 19, 20, 28–35
future of, 208
German World War II efforts,
57–59
Japanese World War II efforts,
59–62
Microbial Therapeutics conference report on, 69–71
overall history of, 1–8, 200–203,
207–208
by pharmaceutical industry,
49–50, 69–70, 71–75, 76
pre-1941 U.S. efforts, 5, 35–36
pure and applied, 199–200, 202
questions in, 6, 203–205
and research safeguards, 32, 206
security regulation of, 44, 54–57
university-based, 204, 205
U.S. support for, 63–66. *See also*
Committee on Medical Research; Northern Regional Research Laboratory; Pharmaceutical industry
- Penicillin, synthesis of. *See also*
Penicillin, analysis of
Beecham replications of, 185–193, 194–195
beta-lactam ring in, 15, 152–157,
159
blocking groups in, 153, 154–157
carbodiimides in, 149, 153, 156,
158, 159
CMR program for, 4, 49, 81,
87–92, 116, 121–122, 161
difficulty in, 6–7, 8–9
industry incentive for, 81–82
Microbial Therapeutics conference on, 70–71
mistaken Portuguese success in,
153, 168–169
need for, 83–84, 86
as organic chemistry example,
92–93
and organic-inorganic gulf,
79–80
- and patent rights, 161–162. *See also* Sheehan, John C., patent applications of
and peptide bonds, 135, 136,
141–142
pessimism over, 1–2, 80, 109–110, 124
post-World War II disinterest in,
16–17, 76, 123–126
reaction toward Sheehan's, 157,
160
renewed 1950s interest in, 127
Sheehan's accomplishment of, 7,
126, 151–160, 172, 176–177,
179
Sheehan's predictions on, 129–134, 207
Sheehan's protected route for,
153, 154, 158–159
Sheehan's unprotected route for,
153–154, 158–159
du Vigneaud's oxazolone-thiazolidine dead end, 115–122
- Penicillin, types of
“penicillin A,” 116
penicillin D, 168
penicillin F, 68
penicillin G, 68, 76, 86, 87,
118–119, 120, 171
penicillin L, 168
penicillin N, 131
penicillin V, 76, 134, 152, 153,
160, 177
- Penicillinase
as penicillin antidote, 134
protecting penicillin against,
131–133
- Penicillin Committee, CMR, 90–91
Penicillium mold
difficulties with, 85
Fleming discovery of, 19, 21–22,
25–26
methods for growing, 66–67
Penicillium chrysogenum, 21
Penicillium notatum, 69, 109
Penicillium notatum (Westling), 21
Penicillium rubrum (Biourge), 21
Penicilloic acid
in analysis of penicillin, 100, 101
and penicillin synthesis, 119
structure of, 101, 133

- Penillic acid
and argument for beta-lactam, 114
in penicillin analysis, 101, 102
structure of, 101
- Penilloaldehyde
in penicillin analysis, 102
structure of, 101
- Pennsylvania State College, research at, 5
- Peoria, Illinois. *See* Northern Regional Research Laboratory, U.S. Department of Agriculture
- Pepper, Senator Claude, 65
- Peptide bonds
and carbodiimides, 137-141, 142-143, 144-145
formation diagram for, 135
and penicillin, 135, 136, 141-142
Sheehan's synthesis of, 135-141, 143-145
- Pfizer Inc.
"admission ticket" of, 75
in CMR synthesis program, 91, 92
in cooperative efforts, 71, 72, 88
early penicillin involvement by, 69
importance of, 201
incentives for penicillin synthesis, 81-82
penicillin sales of, 125
- Pharmaceutical industry
and CMR programs, 4, 69-75, 88, 89-92, 201-202
and CMR task, 49-50
competition in, 73, 202
and cooperative efforts, 71-75, 88, 201
and government researchers, 73-75
interest in penicillin lags, 76, 123, 125-126
interest in penicillin revives, 127
necessary role of, 204-205
and patent rights, 49-50, 72-73, 75-77, 204
- penicillin synthesis incentives of, 81-82
and postwar synthesis efforts, 123, 124-125
- Phenylacetic acid
in penicillin analysis, 102
in penicillin production, 68, 69
- Physical Papers of Henry A. Rowland*, 202-203
- Podbielniak extractor, 85-86
- Prontosil, discovered as antibiotic, 37, 38-39
- Protected route, in Sheehan's penicillin synthesis, 153, 154, 158-159
- Protective groups. *See* Blocking groups
- Raistrick, Harold, 19, 26, 30, 35, 94, 98
- Raney nickel
in biotin analysis, 118
in penicillin analysis, 110, 111
- Rational synthesis
as method, 108, 118
of penicillin, 126, 160, 198
and Sheehan-Beecham patent dispute, 193
- Ratner, 99, 100
- RDX (cyclonite), Sheehan work on, 8
- Reid, Roger D., 5, 35
- Research. *See* Penicillin. research on; Scientific research
- Research Corporation, as Sheehan/MIT representative, 173-174
- Research safeguards
and Oxford group experiments, 32
and penicillin development, 206
- Rhone-Poulenc, Inc., 59
- Rich, Daniel H., 141
- Richards, A. N.
and censorship, 56, 57
as CMR chairman, 45
and CMR program, 48, 69, 70, 71, 91, 164
and Florey, 53
and governmental researchers, 74
and industry incentive, 49
with Merck, 83
and patent rights, 162

- Richards, A. N. (cont.)
and pharmaceutical industry, 72,
75, 88, 202
also 46, 77, 87, 89, 98
Robinson, Sir Robert, 69
on American penicillin contribu-
tion, viii
and Beecham patent claims,
183–184
beta-lactam structure opposed
by, 29, 114, 115
oxazolone-thiazolidine structure
proposed by, 102–103, 108
and penicillin analysis, 94, 98
penicillin synthesis by, 118
personality of, 104–105
Roche Laboratories, in CMR syn-
thesis program, 92
Rockefeller, Nelson, in dedication
ceremony, 176
Rockefeller Foundations, 43, 63,
64, 65
Rolinson, George, 160, 170, 175,
178
Roosevelt, Franklin D., and
OSRD, 44, 45
Rossini, Frederick, 107
Rowland, Henry A., 202–203

St. Mary's Hospital, London, En-
gland, Fleming's work at, 18, 22
Sakaguchi, 178
Sarrett, Lewis, 12
Sayre, Dale N., 188, 189, 190
Schering Corp., 58
Schimmel, Joseph, 181
Scientific research
pure vs. applied, 199–200, 202–
203
questions in, 203–205
rational synthesis as method of,
108, 118
World War II support for, 4,
44–45, 64–65. *See also* Com-
mittee on Medical Research
Security regulation
Anglo-American confusion on,
55–56
CMR measures for, 44, 54–57
vs. free exchange of knowledge,
55

Semisynthetic penicillin
Beecham-Bristol venture in, 160
and patents, 76
and Sheehan research, 127,
151–152, 207
Sheehan, John C.
American Chemical Society
award to, 126
and Beecham, 173, 179–180,
183–192
and Bristol Laboratories, 128–
129, 150, 169, 175–176, 177,
180
carbodiimide research by, 146–
149
career turning points, 9, 10–12,
14–15, 128–129
and Cocoanut Grove disaster, 42
and MIT, 14–15, 135, 145–146,
150–151, 166, 167, 173
and moment of discovery, 2
patent applications of, 166, 169,
173–175, 176, 177–180
patent fights of, xii–xiii, 162,
180–188, 192–197
and patent tests vs. Beecham,
186, 188–192
penicillin predictions of, 129–
134, 207
penicillin purification work by,
86
penicillin research orientations
of, 15–17
penicillin synthesis by, 7, 126,
149–160, 172, 176–177, 179
peptide bonds synthesized by,
135–141, 143–145
personal characteristics of, 145–
146, 150–151
pneumonia-mastoiditis attack of, 8
and Robert Robinson, 108
and semisynthetic penicillin, 127,
151–152, 207
6-APA synthesis by, 126, 154,
157, 159, 179
streptomycin purification by,
12–14
Shell group, beta-lactam study by,
106, 111
Simmons, James Stevens, 45
Singh, Jasbir, 141

- 6-APA (6-aminopenicillanic acid).
 See also Beta-lactam ring
Beecham patent application for,
 173, 178, 179–180, 197
Beecham production of, 126–
 127, 160, 169, 172–173, 179
biological production of, 126–
 127
and Bristol Laboratories, 168,
 169
in fermentation broth, 171–172
and Sheehan patent claims, 162,
 173, 177, 182, 183–185, 193
Sheehan synthesis of, 126, 154,
 157, 159, 179
in Sheehan synthesis of penicil-
lin, 126, 157, 159, 160, 172,
 177, 179
structure of, 133, 159
Smith, Rear Admiral Harold W.,
 45, 46
Southworth, Hamilton, 59
Squibb, E. R., and Sons
 “admission ticket” of, 75
 and Anglo-U.S. cooperation, 53
in “closed corporation,” 73
in CMR synthesis program, 90,
 91, 92
and cooperative research efforts,
 71, 72, 88
early penicillin involvement by, 69
importance of, 201
penicillin purification work by,
 86, 87
penicillin synthesis incentives of,
 81–82
Staphcillin, and penicillinase re-
 sistance, 132
Staudinger, Hermann, 106
Stavely, H. E., 90
Steenbock, Harry, 163
Stereochemistry, in patent test,
 190–191
Stereo-isomerism, and penicillin
 synthesis, 149–150, 151
Stettinius, E. R., Jr., 77
Stevens, Joseph, 11, 83
Stewart, Gordon, 133–134
Stodola, Frank, 98, 106
Stork, Gilbert, 125
Stowell, 173, 177
Streptomycin
 Folkers’s research on, 12
 Sheehan’s purification of, 12–14
Sulfa drugs
 importance of, 79
 in World War II, 3
Sulfanilamide, development of,
 37–39
Sulfonamide, structure of, 39
Sulfur, discovered in penicillin,
 97–99
Surgical sutures, Sheehan research
 on, 148
Synthesis of penicillin. *See* Penicil-
lin, synthesis of
Tanning of leather, Sheehan re-
 search on, 147
Taylor, Elizabeth, penicillin cure
 of, 180
Thiazolidines, and analysis of
 penicillin, 99, 100. *See also*
 Beta-lactam thiazolidine
 structure; Oxazolone-
 thiazolidine structure
Thom, Charles, 21, 65, 71, 72
Thompson, L. R., 45
Thompson, Tommy, 114–115
Time magazine
 on penicillin research, 19, 35
 on Sheehan’s penicillin synthesis,
 157, 160
Tishler, Max
 on beta-lactam, 111
 and Cocoanut Grove, 42
 at Merck, 54, 83, 168
 and penicillin fermentation, 172
 Sheehan helped by, 129, 150
 Sheehan working with, 8, 11
 and streptomycin, 12–13
Todd, Alexander, 89, 137
Trenner, Nelson, 90, 103, 110
Tricyclic formula, Woodward
 proposal of, 107
Umezawa, Hamao, 60
Unprotected route, in Sheehan’s
 penicillin synthesis, 153–154,
 158–159
Upjohn Co., in CMR synthesis
 program, 92

- du Vigneaud, Vincent, 92, 116–118, 120–122, 141
Virus protein, curing of, and Sheehan research, 147–148
- Wallis, Everett, 12
War Production Board (WPB), and synthesis program, 88
Waterman, Robert E., 89
Weaver, Warren, 63
Webb, Jeff, 83, 90, 103, 110, 111, 115
Weed, Lewis H., 45, 55
Wellcome Research Laboratories, 53
Wells, Percy, 65
William Dunn Foundation, 63
William Dunn School of Pathology, 28–29
Wilson, Carroll L., 57, 89
Windus, Charles E., 189, 190
Wintersteiner, Oskar, 86, 87, 90
Winthrop Laboratories, in CMR synthesis program, 92
Wolf, Don, 90, 111, 117
Woodruff, Boyd, 69, 83
Woodward, Robert Burns, 6, 17, 107, 125, 200
World Health Organization, and Podbielniak extractor, 85–86
World War II, penicillin in, 3. *See also* Committee on Medical Research
Wright, Sir Almroth, 22, 27
Wyeth Laboratories, “admission ticket” of, 75
Wylie, Jeff, 167
Wynden, John, 63
- X-ray crystallography, in penicillin analysis, 108–109, 111, 113
X-ray spectroscopy, present effectiveness of, 206
- Yates, Blake, 173, 174