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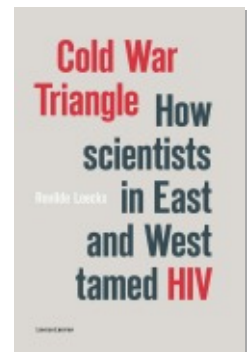
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ALBUM



Intimate ceremony in garden of the Belgian Ambassador in Washington honoring John C. Martin, former CEO of Gilead Sciences and Executive Chairman of the Board of Directors. From left to right: Bill Lee responsible for the second generation of Tenofovir-based drugs of Gilead Sciences, the so-called TAF drugs; Koen Debackere, General Administrator and Vice-rector of the KU Leuven; Dirk Daelemans of the Rega Institute; Thomas Cihlar of Gilead Sciences who developed the TAF- drugs with Bill Lee; Gregg Alton, responsible for Gilead Sciences's reach in countries outside the U.S.; Swami Swaminathan, the mathematics wizzard at Gilead Sciences; Nicolas Gouwy, Representative of Gilead Sciences in Belgium (Photo by Renilde Loeckx).

Notes

Introduction

- 1 As a junior diplomat in Bonn, in the eighties, I was in charge of scientific matters in our embassy. My lack of scientific training was obvious to the German Minister of Science and Technology who put me at ease and reassured me: “Wir sind Alle Juristen.” While serving in the Belgian embassy in Paris in the nineties, French scientists encouraged me to become more vocal about Belgium’s contributions to science. As a Consul-general in New York, I had the honor of hosting Fundraising dinners for Belgian companies involved in Microbicide trials in Africa.
- 2 Renée Fox is the author of *Experiment Perilous*, a classic study of medical research. Her book *In the Belgian Château* not only provides an excellent window into Belgian academic medicine but in the country itself.
- 3 John C. Martin *et al.* (2010) “Early nucleoside reverse transcriptase inhibitors for the treatment of HIV”.
- 4 See Dorothy H. Crawford (2007) *Deadly Companions*.
- 5 Pasteur was a great friend of the English surgeon Joseph Lister and helped him to propagate antiseptic methods for physicians to apply when treating patients. See Paul De Kruif (1926 & 1996) *Microbe Hunters*.
- 6 Anton Van Leeuwenhoek, a Dutch shopkeeper from Delft who in the seventeenth century first uncovered a whole menagerie of “animalcules” as he called the little creatures he saw crawling under his lenses. It was not before the second half of the nineteenth century when some of the secrets of these creatures, which Louis Pasteur termed “microbes”, were unlocked. See Paul De Kruif (1926 & 1996) *Microbe Hunters*.
- 7 Robert Koch, a physician in Berlin, dismissed Pasteur and became his fierce rival. It was as if animosity from the Franco-Prussian war of 1870 had spilled over into their labs. Koch worked on his experiments in a systematic, coldly logical way following his postulates which researchers still abide by to this day. He was hailed as the “father of the microbial theory of disease” for his proving that specific germs caused specific diseases. Koch identified the bacteria

COLD WAR TRIANGLE

- causing anthrax, tuberculosis and cholera but was not able to find a remedy. See Paul De Kruif (1926 & 1996) *Microbe Hunters*.
- 8 While arm-to-arm inoculation or variolation with the virulent smallpox virus was practiced in India and China long before it was introduced in Europe at the beginning of the 18th century. Inoculation sensibly lowered case fatalities of smallpox but the intervention was fraught with danger. See Stefan Riedel (2005) "Edward Jenner (1749–1823) and the history of smallpox and vaccination" *Baylor University Medical Center Proceedings* 18(1):21–25.
 - 9 See Stefan Riedel (2005), *ibid*.
 - 10 See Paul A. Offit (2007) *Vaccinated*.
 - 11 At the dawn of the twentieth century the Dutch microbiologist Martin Beijerinck had isolated the tobacco mosaic virus and found that the virus could only live and propagate in plants. He deduced from a pure chemical analysis that a virus, the smallest of all microbes, had to be a parasite. Knowledge gained many years later showed his vision came surprisingly close to the modern concept of a virus. See A.P. Waterson and Lise Wilkinson (1978) *An Introduction to the History of Virology*.
 - 12 The Enders group's technique is still used to make viral vaccines today. See Paul A. Offit (2007) *Vaccinated*.
 - 13 See John Booss and Marilyn J. August (2013) *To Catch a Virus*.

Chapter 1. Leuven: a hotbed for antiviral research

- 1 Piet De Somer's boss was Richard Bruynoghe, co-owner of a small pharmaceutical company, *Soprolac* which was purchased by a young industrialist, Jacques Lannoy.
- 2 See Alfons Billiau (2009b) "Penicilline in België".
- 3 Fleming's description of *penicillium notatum* is considered as one of the most important medical papers ever written. See also Sir Alexander Fleming's speech at the Nobel Banquet in Stockholm, December 10, 1945 about his findings in the St Mary School in London in 1928, retrieved from http://www.nobelprize.org/nobel_prizes/medicine/laureates/1945/fleming-speech.html.
- 4 The fact that all three major universities in Belgium: Leuven, Brussels and Liège, almost simultaneously offered an honorary doctorate to Alexander Fleming in 1945, underscored their desire to obtain the penicillin formula.

NOTES TO CHAPTER I

- 5 Lannoy's company was first named RIST (*Recherche et Industrie de Synthèses Thérapeutiques*) and later renamed. After the intervention of an angry Parisian doctor of the same name, docteur Rist, it became simply RIT as narrated by one of De Somer's assistants, Alfons Billiau who recorded much of Leuven's medical history.
- 6 In England at that time, penicillin was also made by a dairy company, GLAXO, making use of their old milk bottles. After 1967, RIT became part of Smith Kline and was the steppingstone of Smith Kline's expansion on the continent and its merger with GLAXO, See Alfons Billiau (2009b), "Penicilline in België".
- 7 See de Duve's (2004) speech "The first milligrams of Belgian penicillin" at the festivities for the 50th anniversary of the Rega Institute.
- 8 Professor Joseph Hoet had excellent contacts with Charles Best, the co-discoverer of the insulin hormone (1921) and the Director of Connaught Medical Research Laboratories in Toronto. See Alfons Billiau (2009b), "Penicilline in België".
- 9 Piet De Somer also witnessed a flourishing cooperation between university research and a profitable laboratory created with Charles Best's insulin royalties. See Alfons Billiau (2009), "Penicilline in België".
- 10 Hans Christian Gram, a Danish bacteriologist, found in 1884 that bacteria are divided into two groups. He used a stain and showed that some cells retained the stain and others did not. Those that did not retain the stain, Gram negative bacteria caused diseases like typhoid, tuberculosis and cholera; Gram positive bacteria retained the stain and were bacteria such as staphylococcus, the common cause of blood poisoning against which penicillin is effective.
- 11 The *Laboratoire de Bactériologie* was located in the Vital Decosterstraat in Leuven. See Hubert Vanderhaeghe in De Clercq (ed) (1987) *Frontiers in Microbiology*.
- 12 Waksman had emigrated to America in the waning days of the Russian empire and was welcomed in the Agricultural Department of the Rutgers University. He was well versed in soil bacteria that produced nitrogen available for crops and sold his findings to the brewery and food industries. George Merck, the owner of the pharmaceutical company bearing the same name asked him to look for substances from microorganisms that could treat people. Waksman avoided the topic at first in a similar way he had dodged other opportunities to search for drugs. In 1932 the American National Association Against Tuberculosis had asked Waksman to investigate why tubercle bacilli are

rapidly destroyed in the soil. He simply confirmed that this phenomenon was probably due to the activity of other predator microbes but did not investigate further. Was he afraid to work with the tuberculosis bacteria? His lab was indeed very poorly equipped as described by one of Waksman's biographers. See Peter Pringle (2012) *Experiment Eleven*.

- 13 After Hubert Vanderhaeghe had joined the team with his impressive chemistry skills, De Somer's group developed Griseomycin (in 1953), Virginiamycin (in 1954) and Lo-mycine named after the soil of Kessel-Lo, a village near Leuven. Virginiamycin was later used as a food additive for poultry and swine.
- 14 See Alfons Billiau (2009), "Penicilline in België".
- 15 The Rega Institute was at first composed of three sections. Bacteriology and medicinal chemistry concentrated on the discovery of new antibiotics and new vaccines. A third one was a laboratory entirely devoted to virus research.
- 16 The Belgian provinces in the 1700s were then part of the Austrian Habsburg empire and ruled over by governors from Vienna. Hendrik Rega (1690–1754) a disciple of The Enlightenment enjoyed their trust. He developed the library as a pillar of knowledge. Sciences were then part of the philosophy department and covered wide-ranging interests. See Robert Halleux *et al.* (1998) *Geschiedenis van de wetenschappen in België van de Oudheid tot 1815*.
- 17 Hendrik Rega lived in a palace in the Parijsstraat, 74, in Leuven and is often depicted wearing silk coats, lace cravats and wigs. Rega gave his hometown several buildings like the famous library as well as the anatomy theater, replacing the one that was once used by Vesalius during his studies in Leuven. The botanical garden with the most exotic plants known in his time was another one of his legacies. It all testified to his many talents as a "natural philosopher." See *The History of Medicine Topographical Data* at Himetop.wikidot.com.
- 18 Monique Lamy was the principal assistant who studied equipment and the culturing of the poliovirus in the Danish laboratory of Herdis von Magnus and the laboratory of Pierre Lépine in the Pasteur Institute. See Alfons Billiau (2011) "Piet de Somer, het Leuvense Rega Instituut en het Belgische Poliovaccin in 1956–57".
- 19 In the second half of the twentieth century ten diseases were brought under control thanks to vaccines: polio, measles, mumps, rubella, chickenpox, hepatitis A, hepatitis B, pneumococcus, meningococcus, and Haemophilus influenza type b. See Paul A. Offit (2007) *Vaccinated*.

NOTES TO CHAPTER I

- 20 Awareness of the paralytic poliovirus became more focused when president Franklin Roosevelt started his second term in the White House and American organizations had embarked on a ferocious crusade to combat the virus. Roosevelt himself had become a victim at the age of 39, but the epidemic proportions of the virus only became apparent decades later. See David Oshinsky (2005) *Polio: An American Story*.
- 21 It was likely that this virus had circulated at low levels in human populations for thousands of years. A famous Egyptian stele portraying a priest with a withered leg is testimony to this. The outbreaks only reached epidemic proportions as of the early 1900's when waves of the disease hit cities and rural areas with relatively high standards of living. See David Oshinsky (2005) *Polio: An American Story*.
- 22 Americans saw the germ threat everywhere. Their obsessions with hygiene are amusingly narrated in David Oshinsky (2005) *Polio: An American Story*.
- 23 See Dorothy H. Crawford (2007) *Deadly Companions*.
- 24 Karl Landsteiner successfully isolated the poliovirus in 1908. De Somer had always been fascinated by this Viennese scientist, See Alfons Billiau (2011) "Piet de Somer, het Leuvense Rega Instituut en het Belgische Poliovaccin in 1956-57".
- 25 Salk came from a poor Jewish immigrant background, but was able to attend schools for the gifted. He had worked with his mentor at New York University on experiments with a killed-influenza virus. He built on this experience to inactivate poliovirus with formaldehyde and develop a vaccine in the Medical School of Pittsburgh. See Paul A. Offit (2007) *Vaccinated*.
- 26 Since the poliovirus had been shown to be host-specific—only humans and monkeys were prone to the disease—it was thought it could only grow on human and monkey tissue culture. Enders and his group opened the way for the discoveries of Salk and Sabin thanks to their discovery of the ability of polio-viruses to grow in cultures of various types of tissue. They grew the viruses in test tubes using safe cell cultures. John Enders and his assistants received the Nobel Prize in Medicine in 1954. See Paul A. Offit (2007) *Vaccinated*.
- 27 See David Oshinsky (2005) *Polio: An American Story*.
- 28 De Somer was aided by one of his first assistants, Monique Lamy (1930-2007). She had gained experience in culturing the polio virus with Danish virologist Herdis von Magnus (1912-1992) in Copenhagen and Pierre Lépine

COLD WAR TRIANGLE

- (1901-1989) at the Institut Pasteur in Paris. See Alfons Billiau (2011) “Piet de Somer, het Leuvense Rega Instituut en het Belgische Poliovaccin in 1956-57”.
- 29 Culturing the virus in cells of monkey kidneys was one of Salk’s great innovations. He also pioneered a method for killing the virus without destroying its outer enzyme, see David Oshinsky (2005) *Polio: An American Story*.
- 30 See Alfons Billiau (2011) “Piet de Somer, het Leuvense Rega Instituut en het Belgische Poliovaccin in 1956-57”.
- 31 De Somer’s assistant, Abel Prinzie, was sent to Pittsburgh and worked with Jonas Salk, in Tokyo he befriended Albert Sabin. See Alfons Billiau (2011) “Piet de Somer, het Leuvense Rega Instituut en het Belgische Poliovaccin in 1956-57”.
- 32 To increase the credibility of his vaccines, De Somer wanted to make sure that his testing methods on small chicks acquired the same status as the Danish and Swedish standardized tests on guinea pigs or monkeys. The Rega Institute happened to have an abundance of three week old chicks as they were needed to study the growth potency of new antibiotics. In March 1958, Piet De Somer travelled to Pittsburgh to enlist Salk’s help. The Belgian testing method was introduced to the World Health Organization in Geneva and was formally recognized as equivalent to Swedish and Danish methods soon after. See Alfons Billiau (2011) “Piet de Somer, het Leuvense Rega Instituut en het Belgische Poliovaccin in 1956-57”.
- 33 World EXPO in Brussels took place from April till end of October 1958; the Fair attracted more than fifty million visitors over a period of six months.
- 34 A technique that had been pioneered by Max Theiler when he developed a vaccine against yellow fever in the 1930s. He succeeded in weakening human viruses by growing them in cells from other species. His yellow fever vaccine in mouse embryos in the mid-1930s is still used today. His method has been used for making weakened viral vaccines against measles, mumps, rubella and chickenpox. He won the Nobel Prize in Medicine in 1951. See www.nobel-prize.org.
- 35 Albert Sabin was born in 1906 in Bialystok Poland, then in Imperial Russia. His Jewish family had survived the pogroms but fled the Russian famine during the Bolshevik regime in 1921 and arrived in the US when he was fifteen.
- 36 As the world is coming closer to the complete eradication of polio, the World Health Organization has asked its member countries in 2000 to revert to the killed virus vaccine so as to prevent any propagation of the virus. “In the late

NOTES TO CHAPTER II

1990s, the oral vaccine came in disrepute because of increasing evidence that the attenuated viruses, by replicating in the intestines of vaccinated individuals, can revert to virulence and provoke outbreaks of paralytic polio.” See Alfons Billiau (2014), “A Polio Vaccine for Belgium in 1956”.

Chapter II. Behind the iron curtain

- 1 The pilot of the U2 spy-plane, Gary Powers was taken in captivity. Eisenhower refused a public apology and Khrushchev abandoned his attempts to cooperate with the U.S. and waited for the inauguration in 1961 of the new President, John F. Kennedy.
- 2 *The Pugwash conferences, a staff analysis*, Committee on the Judiciary, U.S. Senate, 1961.
- 3 Scientists from East and West were preparing much of the groundwork for the Limited Test Ban Treaty to be signed a few years later in Geneva.
- 4 The election of a Republican president did not improve the atmosphere at first. Dwight Eisenhower had just entered office and refused to grant a pardon to Julius and Ethel Rosenberg for providing the knowledge of an atomic bomb to the Soviets. The shock of the Rosenberg executions in June 1953 reverberated far beyond the United States. Eisenhower surprised friend and enemy alike, a few months later, with his “Atoms for Peace” speech before the United Nations General Assembly. He spoke of his deep anxiety about an escalating nuclear arms race and the need to warn American people.
- 5 See David Oshinsky (2005) *Polio: An American Story*.
- 6 The fact that DNA holds the key to genetic information in cells is a discovery made by Oswald Avery in 1944. Avery connected Gregor Mendel’s findings with those of another 19th-century discovery by Friedrich Miescher, a twenty-four year-old Swiss student working in a laboratory in the German town of Tübingen. The young student had found a new group of biological substances in the nucleus of the cell. Until then, chemists had classified the principal distinctive substances in living beings into three categories: fats, sugars and proteins. Miescher discovered the fourth one and called it a “nuclein” because he found it in the nucleus of the cell. He later renamed it “nucleic acids.” See Ulf Lagerkvist (2003) *DNA Pioneers and Their Legacy*.
- 7 The Russian invitation to come to Moscow was issued in 1958, the same year the first education exchange agreements between the USSR and the USA

COLD WAR TRIANGLE

entered into effect. In 1957, the Soviets shocked the United States by becoming the first nation to launch a satellite into orbit around the earth. *Sputnik*, as it was called, frightened many Americans, who believed that the Soviets would soon develop an entire new class of weapons that could be fired from space. The Soviets had also sent the immortal He LA cells into space to explore how tissues respond to zero gravity. See Dawn Field and Neil Davies (2015) *Biocode*.

- 8 The first public announcement of what Crick and Watson had found was made before “The Solvay Conference” in Brussels in April 1953, a month after Stalin died. The paper “Molecular Structure of Nucleic Acids: A Structure For Deoxyribose Nucleic Acid” appeared in the April 25th issue of *Nature* (Watson and Crick 1953). Watson presented the structure of DNA in June 1953 at the Cold Spring Harbor meeting on Long Island, one of the birthplaces of modern biology. Crick and Watson had built on Oswald Avery and Erwin Chargaff’s findings and elucidated the structure of the DNA molecule with a model of a double helix. See Horace F. Judson (1996) *The Eight Day of Creation*.
- 9 The base-pairing suggestion was made by Erwin Chargaff in the late 1940’s (Chargaff 1978).
- 10 In 1961, J. Heinrich Matthaei and Marshall Nirenberg published their landmark paper in *Proceedings of the National Academy of Sciences*. They showed that a synthetic messenger RNA made of only uracils can direct protein synthesis. The polyU mRNA resulted in a poly-phenylalanine protein. They had the first piece of the genetic code. By 1966, Nirenberg and his group had deciphered the entire genetic code by matching amino acids to synthetic triplet nucleotides. Nirenberg and his group also showed that with few exceptions, the genetic code was universal to all life on earth. Nirenberg shared the 1968 Nobel Prize in Physiology or Medicine with Har Gobind Khorana and Robert Holley.
- 11 See Harold Varmus (2009) *The Art and Politics of Science*. Varmus was awarded the Nobel Prize for his discovery of the cellular origin of retroviral oncogenes.
- 12 Winston Churchill, speaking in Fulton, Missouri, March 5, 1946: “From Stettin in the Baltic to Trieste in the Adriatic, an iron curtain has descended across the Continent. Behind that line lie all the capitals of the ancient states of Central and Eastern Europe. Warsaw, Berlin, Prague, Budapest, Belgrade, Bucharest and Sofia, all these famous cities and the populations around them lie in what I must call the Soviet sphere, and all are subject in one form or

NOTES TO CHAPTER II

another, not only to Soviet influence but to a very high and, in many cases, increasing measure of control from Moscow.”

- 13 Lysenko's domination of Russian biology continued until Khrushchev's fall in 1964. Later when the noted biochemist Zhores Medvedev wrote the story of Lysenko in 1967 authorities did not react, however reprisals followed for allowing its publication in English in the United States. Medvedev lost his job and became in 1970 the first dissident intellectual to be put into an insane asylum.
- 14 Coming to terms with its past was rendered especially painful in view of the fact that the majority of the country's Jews had been executed in Nazi death camps. After the war, more than two million German-speaking Czechoslovak citizens were punished for their supposed Nazi sympathies. They were forced to seek a new homeland despite their roots in the Czech lands dating back to the 12th century. See Mary Heimann (2009) *Czechoslovakia*.
- 15 František Šorm (February 28, 1913 – November 18, 1980) was a Czech chemist known for synthesis of natural compounds, mainly terpenes and biologically active components of plants. Šorm, the founder of the Institute, studied at the Faculty of Chemistry of the Czech Technical University (later Institute of Chemical Technology, vŠCHT). After the war he returned to the university and in 1946 was named Professor at the vŠCHT. In 1950 Šorm was named Professor of organic chemistry at the Charles University in Prague. In 1952 Šorm became the Director of the Institute. During 1962–69 he served as the second President of the Academy. In the field of bioorganic chemistry, F. Šorm advanced knowledge of sesquiterpenoids, with medium-ring molecules, and explained the structure of different isoprenoid compound. See the website of the Institute of Organic Chemistry and Biochemistry, Prague (<https://www.uoohb.cz/web/structure/637.html?searchString=Šorm&searchId=815>).
- 16 The first genuinely Czech national scientific institution was chartered in 1890, it was closely related to the Royal Bohemian Society of Sciences created by emperor Joseph II in 1784. After the communist party took control of the government in 1948, all scientific, non-university institutions and learned societies were dissolved to make room for the Czechoslovak Academy of Sciences. Czech chemistry was made famous by Bohuslav Brauner of the Prague University who studied rare earth elements and placed them as a separate row at the bottom of Mendeleev's periodic table. See Ulf Lagerkvist (2012) *The Periodic Table and a Missed Nobel Prize*.

COLD WAR TRIANGLE

- 17 A notable chemist from the Academy, Jaroslav Heyrovsky, received the Nobel Prize in chemistry in 1959. Heyrovsky had invented the polarographic method used in chemistry labs the world over, his Polarographic Institute was also brought under the umbrella of the Academy in 1952, see also *Nobel Lectures, Chemistry 1942–1962* (1999).
- 18 See Mary Heimann (2009) *Czechoslovakia*.
- 19 In his *Recollections* (1994) Otto Wichterle (1913–1998) explains why he and his colleagues did not engage in the reform movement in its early phase.
- 20 See Jan Vilcek (2015) *Love and Science*.
- 21 See Zhores A. Medvedev (1969) *The Rise and Fall of T.D. Lysenko*.
- 22 Milan Hašek came close to the Nobel Prize. The prize was awarded instead to Peter Medawar and Burnet in 1960.
- 23 See Juraj Ivanyi (2003) “Milan Hašek and the discovery of immunological tolerance”.
- 24 Quote from František Šorm, the second president of the Academy of Sciences: *The character of science is international; the results of research are in essence a synthesis of the work of scientists from all over the whole world, resulting from their close mutual cooperation or exchange of experiences. For that reason, we stand for completely free contacts of scientists in all countries and of course also that all the scientific works would be published and be public. Science is the property of the whole of humanity*. Quote researched and translated by Riika Nisonen-Trnka (2010).
- 25 See Horace F. Judson (1996) *The Eight Day of Creation*.
- 26 Interview with Prof. Marc van Montagu.
- 27 See Zhores A. Medvedev (1969) *The Rise and Fall of T.D. Lysenko*. The author was punished when this book was published in the United States, he was the first Russian scientist to be sent to an asylum in 1970. Fortunately many scientists from all over the world united in their protests to Soviet authorities, he was liberated and sent into exile instead.
- 28 Hašek would pay a heavy price as late as 1970 when he would be stripped of his membership in the party and his Directorship of his institute.
- 29 His connection with industry made him an attractive target for Stanford’s energetic provost working to bring the best and the brightest to Silicon Valley. The provost coaxed Djerassi and his whole group of collaborators into moving to Palo Alto, as was often done with other esteemed scientists, Nobel Prize winners and their teams.

NOTES TO CHAPTER III

- 30 1964 was a landmark year. The growth of foreign academic exchanges contacts with capitalist countries, in particular in natural sciences, was extraordinary. Czechoslovakia had more extensive scientific projects going with Western countries than any of the other communist countries. The slow, inefficient intra-bloc collaboration had pushed Czechoslovakia inexorably towards more Western cooperation.
- 31 At first, the increase in Western contacts was depicted as a by-product of the overall improvement of international scientific cooperation. See Riikka Nisonen-Trnka (2010) “The Prague Spring of Science”.
- 32 Otto Wichterle’s licence was sold to a small American company, National Patent Development Corporation which hitherto had been focusing its interests in technology available in the Soviet Union
- 33 In Carl Djerassi’s words “instead of poisoning the bug, one might interfere with a natural process for survival such as molting. A group in Šorm’s laboratory had been working on the chemistry of insect hormones and we had initiated a collaborative research program between Zoecon and the Czech Academy [...]” See Carl Djerassi (1992) *The Pill, Pygmy Chimps, and Degas’ Horse*.
- 34 See Antonín Holý (2006) “*My Life With Nucleic Acid Chemistry*”.

Chapter III. Strange bedfellows: a Czech chemist and a Flemish virologist

- 1 Antonín Holý studied organic chemistry at the Charles University in Prague from 1954 to 1959.
- 2 See Antonín Holý (2006) “*My Life With Nucleic Acid Chemistry*”
- 3 Antonín Holý’s assistant was Mrs. Bela Novakova.
- 4 Sir Alexander Todd had received a Nobelprize in 1957 for his work to trace the fundamental chemical structure of nucleic acids, the material that passes genetic characteristics from mother cell to the offspring.
- 5 As its new name revealed, a new department of Biochemistry was added to the Institute, the Director was Šorm’s spouse, Zora.
- 6 See René Thomas (1992) “Molecular Genetics Under an Embryologist’s Microscope”.
- 7 Both Brachet and the Swedish scientist, Caspersson, amassed evidence for a role of RNA in “protein synthesis” in 1939 that was definitely proven about twenty years later. They were nominated for a Nobel Prize several times, with

COLD WAR TRIANGLE

- a thorough review of their contributions by the Nobel Committee in 1959. See *Nobel Prizes and Life Sciences* by Norrby, E.
- 8 The Nazis imprisoned Jean Brachet together with several other professors of the Brussels University in a fortress in Southern Belgium. They all had communist ties and refused to reveal which one among their colleagues was Jewish.
- 9 Antonín Holý also received an honorary doctorate from the Ghent University.
- 10 The USA became another important scientific partner next to Germany. Scientists were discretely encouraged to emigrate to the US. See Riikka Nisonen-Trnka (2010) “The Prague Spring of Science”.
- 11 SAFIA: Société Anonyme pour Favoriser l’Industrie Agronomique.
- 12 Erik and his father often walked through the neighboring village, Sint Amands, the home of the Flemish author and poet Emile Verhaeren. The French admired his mastery of the French language and wanted to immortalize Verhaeren’s remains in the Pantheon in Paris. According to his wishes, Verhaeren was buried in the banks of the Scheldt so that even in death he could feel the tides of the river.
- 13 “Lysosomes are like the rooms within a cell” dixit Prof. Erik De Clercq.
- 14 The laboratory was headed by prof. Raymond Devis.
- 15 Steroid hormones help control metabolism, inflammation, immune functions, sexual developments, water balance and the ability to withstand illness and injury. Catecholamines are hormones produced by adrenal glands in response to physical or emotional stress.
- 16 An instrument used in chemistry analysis to measure light reflections.
- 17 By the mid-sixties geneticists could confirm what had been innate wisdom for centuries. Each time an infectious disease hit our ancestors it weeded out the weakest, leaving only the more resistant survivors to pass on their genes to future generations. Thus step by step, a long line of forebears who survived disease spawned offspring with genetic resistance to a whole range of microbes. These battles taught microbes to restrain their virulence so as not to kill their host outright while at the same time to avoid being conquered by the human’s immune system. Of the million or so microbes in existence, only 1,415 are known to cause disease in humans. See Dorothy H. Crawford (2007) *Deadly Companions*.
- 18 Cfr. Erik De Clercq’s recollections.

Chapter iv. The sixties in Leuven and Prague

- 1 Virus interference had first been described in 1937 by British virologist Fred Mac Callum. Virus interference as a biological phenomenon referred to the blockage by one virus of the growth of another virus when both try to infect the same cells. In the 1940s new techniques revealed that a virus could retain its capacity to ‘interfere’ even when it has itself been inactivated. The interference phenomenon remained nevertheless shrouded in mystery. See Toine Pieters (2005) *Interferon: Science and Selling of a Miracle Drug*.
- 2 Werner and Gertrude Henle studied this phenomenon in 1943 in Philadelphia. In *The Story of Interferon* Kari Cantell (1998) speculates that the Henle’s could have found interferon first if they had used small bits of membrane of the fertilized chicken egg rather than whole eggs containing a fertilized embryo. In post-war England these were in short supply. Isaacs and Lindenmann substituted for the use of a whole embryonated egg embryonic membrane cultures. One single egg used sparingly would provide many pieces of the embryonic membrane. Isaacs was also in charge of the World Influenza Centre in Mill Hill, influenza viruses greatly aided his work on interferon.
- 3 See Derek Burke (2009) “The Discovery of Interferon, the First Cytokine, by Alick Isaacs and Jean Lindenmann in 1957”.
- 4 See Derek Burke (2009), *ibid*.
- 5 One of Isaacs’s letters to Lindenmann underscores this point. See Toine Pieters (2005) *Interferon: Science and Selling of a Miracle Drug*.
- 6 Derek Burke recalled that Isaacs received a letter from John Enders in June 1959 in a state of euphoria. See Toine Pieters (2005) *Interferon: Science and Selling of a Miracle Drug*.
- 7 See interview with De Somer’s assistant, Edward De Maeyer, in Sandra Panem (1984) *The Interferon Crusade*.
- 8 An honorary doctorate five years before his untimely death, Isaacs died in January 1967.
- 9 See Jan Vilcek (2015) *Love and Science*.
- 10 Cantell’s work was downplayed by those who were working with fibroblasts as they pointed out the possibility that viruses present in the donor blood might be transmitted to and cause disease with the recipients. See Kari Cantell (1998) *The Story of Interferon*.

- 11 When De Somer's assistant, Edward De Maeyer, tried to row upstream and publish some of his findings, he received rejection letters from both *Virology* and *Science* on the grounds that the material under study was ill-defined and impure and therefore of no great scientific interest. See Toine Pieters (2005) *Interferon: Science and Selling of a Miracle Drug*.
- 12 Piet De Somer *et al.* (1967) "Urinary excretion of interferon in rabbits".
- 13 Piet De Somer *et al.* (1968) "Antiviral activity of polyacrylic and polymethacrylic acids".
- 14 See Toine Pieters (2005) *Interferon: Science and Selling of a Miracle Drug*.
- 15 Maurice Hilleman made or improved twenty vaccines for the Merck company. See Paul A. Offit (2007) *Vaccinated*.
- 16 See Michael Žantovský (2014) *Havel: A Life*.
- 17 The radio broadcast condemned "the occupation by the armies of the Warsaw Pact as a flagrant transgression of the principles of international law and state sovereignty which damages the cause of socialism in the eyes of all the nations of the world." See Mary Heimann (2009) *Czechoslovakia*.
- 18 Quote from Jaroslav Kožešník, the third president of the Academy of Sciences. See Stanley B. Winters (1994) "Věda a politika: vzestup a pád Československé Akademie Ved [Science and Politics: The Rise and Fall of the Czechoslovak Academy of Sciences]".
- 19 A minor planet (3993 Šorm) was named after him in 1988 by his friends in the West. The IOCB now awards a medal named after František Šorm. Cfr website IOCB. Carl Djerassi named a sterol after Šorm, Šormosterol. See Carl Djerassi (1992) *The Pill, Pygmy Chimps, and Degas' Horse*.
- 20 Holý, Antonín (1967) "Synthesis of 5'-deoxyuridine 5'-phosphonic acid".
- 21 See Stanley B. Winters (1994) "Věda a politika: vzestup a pád Československé Akademie Ved [Science and Politics: The Rise and Fall of the Czechoslovak Academy of Sciences]".

Chapter v. Enzymes: the secret of life as chemistry

- 1 Erik De Clercq had an Eli Lilly fellowship for one year in Stanford and prolonged his stay for a second year with a Damon Runyon fellowship.
- 2 Hilleman's articles appeared in the prestigious *Proceedings of the National Academy of Sciences* in 1967. Each article revealed a different method to obtain double stranded RNA, a rare commodity. It could be found in certain molds or

NOTES TO CHAPTER V

- in a reo virus or it could be synthesized in the laboratory imitating the chemical building blocks of RNA into poly nucleotides. (poly I:C).
- 3 The more common function for RNA is to read the double stranded DNA and translate it into a single strand to direct the cell in its protein production.
 - 4 Around 1966, Merigan and De Clercq had discovered, independently from each other, that some synthetic polymers had antiviral activity.
 - 5 Eckstein had sent copolymers that happened to be sulfur bearing RNA, compounds similar to those Maurice Hilleman had discovered.
 - 6 See the article “Modified RNA Aids Fight against Viral Diseases” in *Chemical & Engineering* of June 1969.
 - 7 Growing up in a poor Jewish neighborhood of New York City, Kornberg (1919–2007) gained a degree in medicine, became a ship’s doctor during wartime, and had published a brief study on jaundice and vitamins or coenzymes. This caught the attention from the NIH who hired him to work on coenzyme synthesis despite his lack of formal training in science. Kornberg became the chair of the microbiology department of the University in St Louis where he found the enzymes that assemble nucleotides into RNA or DNA. This brought him to the attention of Stanford’s provost who asked him to set up a new school of biochemistry on the Stanford campus. Kornberg was allowed to hire all his former co-workers and brought his team of 22 people with him to Stanford in 1959. Shortly after he started his tenure he was awarded the Nobel Prize in Medicine. See *Profiles in Science* of the NIH (<https://profiles.nlm.nih.gov/>).
 - 8 See Arthur Kornberg (1989) *For the Love of Enzymes*.
 - 9 Arthur Kornberg repeats a citation of De Clercq (1979) in his handbook *DNA Replication* (Kornberg 1992).
 - 10 Their merger was the steppingstone for Smith Kline’s expansion on the continent and later for a conglomeration with Glaxo. Today, Glaxo Smith Kline is the largest vaccine producer in the world. The vaccine based on the Cendehill strain is still the vaccine of choice in many parts of the world for MMR vaccination against rubella in combination with the measles and mumps virus vaccine. See Alfons Billiau (2011) “Piet de Somer, het Leuvense Rega Instituut en het Belgische Poliovaccin in 1956–57”.
 - 11 SKF became what is today the GlaxoSmithKline giant. SKF did not like the Rega Institute’s emphasis on interferon research. See interview with Piet De Somer in *Knack Magazine*. SKF itself had abandoned its activities in this field by 1970. See Sandra Panem (1984) *The Interferon Crusade*.

COLD WAR TRIANGLE

- 12 De Clercq's technical aide was Anita van Lierde, she remained his faithful assistant till the end of her career.
- 13 The conference is chronicled in Kari Cantell (1998) *The Story of Interferon*.
- 14 Tom Merigan showed that interferon could affect the course of chronic hepatitis B infections in 1975. It opened the road for interferon to become a routine treatment for the various forms of chronic hepatitis. See Kari Cantell (1998) *The Story of Interferon*.
- 15 Erik De Clercq was teaching biochemistry in Kortrijk, a regional campus of the KU Leuven as of 1972. He climbed up the academic ladder and was named full Professor in 1977.
- 16 See the articles by Sol Spiegelman in the PNAS.

Chapter vi. From interferon to nucleosides

- 1 The Ghent University had conferred an honorary doctorate to David Shugar in 1969.
- 2 The Errera House Rue Royale, 14 Brussels, is presently the official residence of the Flemish Government.
- 3 The organizers were the Max Planck Institut für Biophysikalische Chemie and the Max Planck Institut für Experimentelle Medizin.
- 4 See photo with list of participants.
- 5 The first antiviral drugs developed in the late fifties and early sixties were: idoxuridine, vidarabine, trifluridine and ribavirin.
- 6 See Antonín Holý (2006) "My Life With Nucleic Acid Chemistry".
- 7 The technician was Anita Van Lierde.
- 8 The name, herpes, is derived from the Greek word "herpeion," meaning reptile in likely reference to the creeping nature of the herpes lesions. See Dorothy H. Crawford (2011) *Viruses*.
- 9 The compound, Acyclovir, was first synthesized by the US branch of the Wellcome company and its antiviral activity discovered in the UK parent company.
- 10 There are three herpes subfamilies; alpha, beta and gamma categorized according to the cell types in which they establish latency. So far eight human herpes viruses have been discovered named HHV 1 to 8 in order of their discovery. They also have been given common names by which they are more familiarly known, herpes simplex, varicella zoster, Epstein-Barr,

NOTES TO CHAPTER VII

cytomegalovirus, Kaposi sarcoma associated herpes virus. See Dorothy H. Crawford (2011) *Viruses*.

- 11 Peter Langen was Department Head at the Institute of Biochemistry in East Germany (Berlin-Buch). An Institute that was placed under the umbrella of the Academy of Sciences of the GDR.
- 12 The conference was sponsored by the Federation of European Biochemistry Societies (FEBS) and co-organized with the IOCB of the Czechoslovak Academy of Sciences.
- 13 East Germany would become BVDU's lifeline. Finding an industrial partner in the West in order to translate the compound into a drug was fraught with misunderstandings. The drug was first produced in the early eighties in East Germany for immunosuppressed patients. BVDU—under the brand name Helpin—became available for all other patients and in the whole of Germany once the Berlin Wall fell in 1989. A comparative clinical trial in Erfurt 1995 showed that BVDU is many times more powerful than acyclovir.

Chapter VII. Breaking away from interferon

- 1 See Kari Cantell (1998) *The Story of Interferon*.
- 2 The Fifth Aharon Katzir-Katchalsky Conference: Symposium on Interferons and The Control of Cell-Virus Interactions, Rehovot, Israel, May 2–6, 1977.
- 3 The term, cytokine, was derived from the Greek words *kytos* for cell—inspired by the fact that these proteins are both derived from cells and act on cells—and *kine* referring to the proteins moving the immune system into action. It was not known then that hundreds of cytokines have been discovered in recent decades. See Jan Vilcek (2015) *Love and Science*.
- 4 Biogen was saved from bankruptcy in 1979 once it agreed to assign its future interferon patents to a pharma company, Schering-Plough. See Kari Cantell (1998) *The Story of Interferon*.
- 5 Maurice Hilleman wanted to find some nucleic acid or polynucleotide which could be used as a drug in humans. Poly I: C was a highly effective inducer in cell cultures and animals, but proved inactive in man because human blood contains an enzyme which breaks it down. When a stable form of poly I: C was developed, it was found that this was quite toxic to man. See Kari Cantell (1998) *The Story of Interferon*.

Chapter VIII. The first antiviral drugs

- 1 The NATO Advanced Study Institute in Corfu was organized by Prakash Chandra, head of molecular medicine at the University Medical School in Frankfurt.
- 2 Gallo's quest actually succeeded not so long after their meeting. In 1980 Gallo found a retrovirus that caused leukemia in humans he would find a second one in 1982 and unfortunately the third one, the one that causes AIDS is the one that got him embroiled as of 1983 in a Transatlantic dispute with his French colleagues.
- 3 Erik De Clercq found in 1975 that suramin was active against the Moloney murine leukemia retro virus. This was later seen as the first line of defense against the virus causing AIDS (Mitsuya *et al.* (1984) "Suramin protection of T cells in vitro against infectivity and cytopathic effect of HTLV-III.>").
- 4 This NATO Advanced Study Institute took place in Sogesta, Italy and was held from 7–18 May, 1979.
- 5 See Richard T. Walker, Erik De Clercq and Fritz Eckstein (eds.) (1979) *Nucleoside Analogues*.
- 6 According to Arthur Kornberg, the di-deoxy nucleotides—much the same as the nucleotide building blocks of DNA, but lacking the chemical group that would allow them to be linked into a chain—that emerged from the work at Syntex were invaluable to two Nobel Prize winners: himself in his studies of the DNA polymerase action, which, in turn, inspired Fred Sanger to use them in his celebrated procedure for sequencing DNA.
- 7 John Moffatt's graduate work with Khorana dealt with the synthesis of phosphate compounds. See Arthur Kornberg (1995) *The Golden Helix*.
- 8 Gobind Khorana (1922–2011) had a late start in science. He grew up in the only literate family in a Punjabi village of one hundred people. Monthly visits by an itinerant teacher were hardly the preparation he needed for a university curriculum but he managed to graduate at a Punjab University and obtain a doctorate in Liverpool. It was in Cambridge with Sir Alexander Todd that he developed an interest in proteins and nucleic acids. He shared the Nobel Prize in 1968 with Marshall Nirenberg for establishing that the biological language common to all living organisms, is spelled out in three-letter words: each set of three nucleotides codes for a specific amino acid. See DNA Learning Center, Cold Spring Harbor laboratory.

- 9 Prusoff synthesized the first antiviral used in clinical practice, a drug called idoxuridine that treats herpes infection in the eye. It is a synthetic nucleoside.

Chapter IX. AIDS emerges in the shadow of the cold war

- 1 The “Charité” is an impressive 300-year old university hospital built by King Fredric II of Prussia.
- 2 See George Packer (2014) “The Quiet German”.
- 3 Roald Hoffmann shared the Nobel Prize for chemistry in 1981 with a Japanese chemist, Kenichi Fukui.
- 4 See Hans-Jörg Schmidt (2013) “Wie Merkel Filzpantoffeln nach Prag schmuggelte”.
- 5 See Hartmut Wewetzer (2013) “Bundeskanzlerin Merkel ehrt ihren akademischen Lehrer Rudolf Zahradnik”.
- 6 See Angela Merkel *et al.* (1988) “Evaluation of the rate constant for the SN2 reaction flouromethane+hydride → methane+fluoride in the gas phase”.
- 7 See Hartmut Wewetzer (2013) “Bundeskanzlerin Merkel ehrt ihren akademischen Lehrer Rudolf Zahradnik”.
- 8 The Centers for Disease Control and Prevention, the leading national public health institute of the United States based in Atlanta, see their *Morbidity and Mortality Weekly Report of 5th June 1981*.
- 9 The documentary by Michael Isikoff (2015) *Uniquely Nasty: The U.S. Government’s War on Gays*.
- 10 The frustration was big enough for Whitley and Martin to start thinking about creating a nucleosides network of their own. One without a limitation of American participants. This was achieved with the annual ICAR conferences of the International Society for Antiviral research (ISAR) they had founded in the mid 1980s.
- 11 See Sandra Panem (1988) *The AIDS Bureaucracy*.
- 12 See Dorothy H. Crawford (2011) *Viruses*.
- 13 The viruses causing leukemia, HTLV-I and HTLV-II, provoked an erratic and out-of control growth of white blood cells while the AIDS virus did quite the opposite. It attacked and destroyed white blood cells that normally protect the body’s immune system.
- 14 See Leonard Norkin (2014) “How The Human Immunodeficiency Deficiency Virus (HIV) Got Its Name” and Morton A. Meyers (2012) *Prize Fight*.

- 15 See Guido Van der Groen (2015) *In het spoor van Ebola*.
- 16 The mission to Zaire as the Democratic Republic of Congo was known then, was funded by the NIAID with a contribution from the Institute for Tropical Medicine in Antwerp.
- 17 It allowed the Antwerp group to set up the first AIDS project in Africa, the projet SIDA in Kinshasa.
- 18 Two antibody tests had been developed by 1985 that, if used together, were capable of screening out nearly all individuals infected with HIV. The first test, *enzyme-linked immunosorbent assay (ELISA)* allowed for many false positives, but when followed up with a second test, the *Western Blot*, that showed more false negatives, they were nearly 100% accurate. See Jonathan Engel (2006) *The epidemic*.
- 19 See Jonathan Engel (2006) *ibid*.

Chapter x. From passivity to action

- 1 Sakuma's systems to test the varicella-zoster virus and tests for the cytomegalovirus originated in the Asahikawa University on Hokkaido, Japan.
- 2 De Somer's speech about the "right to err," to stray from the dogmatic (Catholic) course and to change accepted standards was perceived as insubordination against the authority of the Church.
- 3 A Scientist at Burroughs Wellcome, Phil Furman, had found AZT's chemical structure, so the company was awarded the "method-of-use" patent.
- 4 Ironically, PMEA is precisely the compound that revealed its anti-HIV activity in 1988 (at the hands of Rudi Pauwels).
- 5 The fact that Hudson and hundreds of other Americans were seeking medical treatment outside the US—in France alone more than four hundred pleading for help—to receive Montagnier's experimental AIDS drug was a sneer to American healthcare. Secretary of Health Heckler announced the drug would be available in the US for "compassionate" use within 3 weeks.
- 6 Senator Jesse Helms attached anti-gay Amendments in appropriation bills one after another. The amendments blocked prevention measures and limited research.
- 7 Berlin Chemie, the industrial patron of De Clercq's friends, became part of the global Italian Menarini group, based in Florence, after the Fall of the Wall. It was a new take-off for the drug and a source of royalties for the University in Leuven from 1990 to 2002. The drug was known under different names:

NOTES TO CHAPTER XI

Helpin or Zostex in Germany, Brivirac in Italy, Zerpex in Belgium. It is now available in large parts of the world including China.

- 8 Blough, H.A. *et al.* (1986) “Glycosylation inhibitors block the expression of LAV/HTLV-III (HIV) glycoproteins”.
- 9 The article was sent to Madrid in November 1986 and published in the Biochemical, Biophysical Research Communications (BBRC) of January 17, 1987. See Masanori Baba, *et al.* (1987) “Both 2',3'-dideoxythymidine and its 2',3'-unsaturated derivative (2',3'-dideoxythymidinene) are potent and selective inhibitors of human immunodeficiency virus replication in vitro”.
- 10 See William Prusoff (2001) “The Scientist’s Story”.
- 11 The final patent, use for treatment of HIV infection, was granted to Tai-shun Lin and William Prusoff in 1990. See John C. Martin *et al.* (2010) “Early nucleoside reverse transcriptase inhibitors for the treatment of HIV”.

Chapter XI. First attempts to halt the epidemic

- 1 Janssen founded his research laboratory in 1953 within his father’s company with a loan of three thousand dollars from his father. He also discovered his first drug ambucetamide that same year. In 1956 he established the company which would become Janssen Pharmaceutica. In 1958 he made haloperidol, a major breakthrough in schizophrenia and with his team he developed the fentanyl family of drugs and many other anesthesia-related drugs before the merger with J&J in 1961.
- 2 See Geerd Magiels (2008) *Paul Janssen*.
- 3 See Jonathan Engel (2006) *The epidemic*.
- 4 President Reagan and Prime Minister Jacques Chirac ended the scientific dispute between France and the U.S. They signed an agreement on March 31 about the sharing of credit for the discovery of HIV. The patent rights to a blood test that emerged from that discovery would also be shared with most of the royalties donated to a new foundation for AIDS research. The settlement contained a seven page chronology specifying the contributions of each, of Montagnier as well as of Gallo.
- 5 See Laurence K. Altman (1987) “U.S and France end Rift on AIDS”.
- 6 Luc Montagnier was also awarded an honorary doctorate in 1987 by the Leuven University, on a separate occasion.

COLD WAR TRIANGLE

- 7 Galasso was the driving force behind the III international Conference on AIDS that took place a few weeks later in Washington DC, with Vice president George H. Bush as one of the main speakers. The conference assembled more than 6,000 participants.
- 8 Adefovir dipivoxil or Hepsera as the PMEA compound was known was the second anti-HBV drug for the treatment of chronic hepatitis B. It proved active against those HBV strains that were resistant to lamivudine, the first anti-HBV drug.
- 9 HPMPC consists of cytosine instead of adenine, it was first described in 1987 and approved in 1996 for retinitis in AIDS patients under the brand name Vistide.
- 10 Gertrude Elion had easy access for publishing through the prestigious National Academy of Sciences. She explained in her articles that acyclovir masqueraded as a nucleoside, a building block of DNA, in order to be incorporated into the herpes virus DNA and prevent it from further using the cell's machinery to replicate. (Gertrude Elion *et al.* (1977), "Selectivity of action of an antiherpetic agent, 9- (2-hydroxyethoxymethyl)guanine").
- 11 In 1988, Gertrude Elion of Burroughs Wellcome (now GlaxoSmithKline) received the Nobel Prize in Medicine along with George Hitchings and Sir James Black for "their discoveries of important principles in drug treatment." Gertrude Elion's name was indelibly associated with Acyclovir.

Chapter XII. Finding the best therapy: the one-a-day-pill

- 1 Paula Pitha had earned her Ph.D under the directorship of František Šorm at the IOCB in Prague. She hosted an event for Erik De Clercq's lecture at Johns Hopkins in 1970, after he left Stanford University. Cf. chapter V.
- 2 The company was incorporated under a place-holder name and then officially changed to Gilead Sciences a few months later, in early 1988. Michael Riordan came across "Gilead" when he read a play by the American playwright Lanford Wilson, called "Balm in Gilead." He found that the balm is an extract from certain trees indigenous in a region of the ancient Middle East called Gilead, near the Jordan River. The balm of Gilead was probably one of mankind's first genuine therapeutics. Riordan added "Sciences" to the name to make clear the company was based on rigorous research and scientific principles.

NOTES TO CHAPTER XII

- 3 A former Gilead scientist, Jeff Bird, spoke with reporters, about the early days of Gilead. See Denise Gellene “Gilead’s Research Goes to Front Lines”.
- 4 Benno C. Schmidt Sr. (1913 – 1999) was an American lawyer who is credited with coining the term venture capital. See *Richard A. Oppel Jr (1999) “Benno C. Schmidt, Financier, Is Dead at 86”*.
- 5 Etienne (Stevie) Davignon, was a former Belgian diplomat and former Member of the European Commission. The common bond between Rumsfeld and Davignon was Stevie’s mentor, the legendary Belgian ambassador at NATO and one time confidant of Winston Churchill, André de Staercke. He had joined Rumsfeld’s board at Searle but was rapidly advancing in age and deferred to his friend, Davignon.
- 6 Gilead’s Initial public offering was of 5.75 million common shares of stock. The IPO was completed, with proceeds of \$86,25 million.
- 7 Erik De Clercq had convinced Paul Janssen to travel to Oxnard, California to participate in the session devoted to “the non-nucleoside anti-HIV drugs.” The topic was close to his heart, since they were precisely his compounds that Rudi Pauwels and Dominique Schols had been so doggedly working with in the Rega Institute.
- 8 Gancyclovir was still not approved by FDA but it had saved many people already who were on the drug in parallel circuits.
- 9 Robert Snoeck had done all the screenings and testings in the clinic. Another of De Clercq’s coworkers, an Argentinian researcher, Graciela Andrei, found many other properties of cidofovir including one to treat cancer caused by HPV. De Clercq met Graciela Andrei at a conference in Mar del Plata and enticed her to work with him. She had received some special training at the University of Alabama to work with the human papilloma viruses, a very large family of viruses with over 100 different types, a few types can cause cancer but can be treated in the clinic with *cidofovir*.
- 10 Compounds from the IOCB in Prague were handled in the Rega Institute by Jan Balzarini, Dominique Schols and Lieve Naessens.
- 11 The three protease inhibitors were produced by Merck (which made Crixivan), Abbott (Norvir), and Hoffman-La Roche (Invirase).
- 12 The center was created by Irene Diamond in memory of her husband who left her several hundred millions of dollars upon his death, Irene Diamond was famous for her production of the movie “Casablanca.” See Jonathan Engel (2006) *The epidemic*.

- 13 Viread and Emtriva were marketed as single drugs and patients were required to take other Antiretrovirals. Similarly patients taking Truvada had to also take either a Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI) or a protease inhibitor (PI).

Epilogue: Of scientists and crusaders

- 1 Peter Piot, em. professor at the Institute of Tropical Medicine in Antwerp, he became Assistant Director of the World Health Organization's Global Programme on HIV/AIDS. He was appointed Executive Director of the Joint United Nations Programme-UNAIDS and Assistant-Secretary-General of the United Nations (1994-2008).
- 2 The Security Council adopted Resolution 1308 in July 2000, stating that there should be no UN peacekeeping operations without HIV prevention.
- 3 See Peter Piot (2015) *AIDS Between Science and Politics*.
- 4 See Joe Conason (2016) *Man of the World: The Further Endeavors of Bill Clinton*.
- 5 The World Health Organization estimates that HIV has claimed more than 35 million lives so far and that approximately 36.7 million people were living with HIV at the end of 2015. By mid-2016, 18.2 million people living with HIV were receiving antiretroviral therapy. See Media centre HIV/AIDS of the World Health Organization.

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COLD WAR TRIANGLE

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