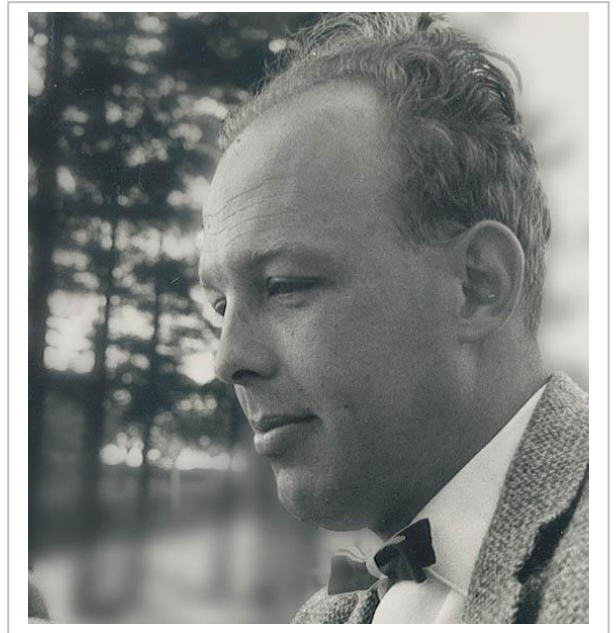


Bart Helmich Rispens

1929 – 1973



Prepared by: K.A. Schat, Jan Albert Rispens and
Babs Landman-Rispens

Date: February 7, 2025

XX

THE CONTRIBUTIONS OF DR. BART RISPENS TO POULTRY HEALTH

Introduction. The poultry industry is very familiar with the CVI-988, also known as “Rispens vaccine,” to protect chickens against Marek’s disease. It is still considered to be the “gold standard” for single MD vaccines. Yet, few people are familiar with the life story of Bart Rispens. The purpose of this biography is to provide an overview of his life and contributions to poultry health.

The person Bart Rispens. Bart was born in Deventer, The Netherlands on May 10, 1929, to Margaretha Rispens-Klaver and Dr. Jan Albertus Rispens (12-5-1889 – 3-27-1962). Jan Albertus received his PhD from the University of Utrecht studying Dutch and philosophy, published at least

ten books, and worked as a teacher in the Deventer High School system. Jan had a major impact on the intellectual development of Bart. His younger brother Pieter Albert was born on 2-27-1935 but passed away on 11-8-1944. There is little information available about Bart's younger years. Fig. 1 shows Bart when he was 11 years with his younger brother, who died during the war by an infectious disease. During the Second World War Bart went outside his house to meet a friend and a few minutes later the outside wall of his bedroom was hit by a shell. After 3 years of High School, Bart matriculated in the College of Tropical Agriculture in Deventer with idea to work afterwards at the sugar cane plantations in the Dutch Indies (now Indonesia). Fortunately for the poultry industry he changed directions and enrolled in 1949 at the College of Veterinary Medicine of the State University of Utrecht. He received his DVM degree in 1956. During his years in Utrecht, he met Wihelmina Johanna Adriana (Will) Agerbeek (2-21-1935 -1-27-2021). Bart and Will got married in 1959 (Fig. 2). Their marriage was blessed with two children: Jan Albert and Babs.



Fig.1. Bart with Pieter

In 1966, he received his PhD degree from the State University in Utrecht under the mentorship of Professor A. van der Schaaf, while he was working at the Central Veterinary Institute. The final exam for obtaining a PhD degree in The Netherlands is a formal affair taking one hour (Fig. 3). Unfortunately, Bart became quite ill in 1970 and passed away on November 11, 1973 at the age of 44 years.

Dr. Rispens: The Scientist. Directly after receiving his DVM degree in 1956, Dr. Rispens joined the “Rijksseruminrichting” which changed to Central Veterinary Institute (CVI), division Rotterdam in 1959. The facilities were suboptimal with an old-fashioned main building (Fig. 4.A) and a small wooden building (Fig 4.B) where Dr. Rispens and his team worked. In 1972, the virology department of CVI moved to a new modern facility in Lelystad. Unfortunately, he only enjoyed the new facility for a short time. Dr. Rispens had an intuitive feeling for research with an emphasis on projects benefitting the poultry industry. To quote his former co-worker Dr. H.J.L. Maas: “*Working to improve the economic situation of the poultry producers is enriching my life*” (1).



Fig. 2. 1959: The wedding picture of Bart and Will



Fig. 3. 1966: Dr. Rispens receives his PhD degree from Professor A. van der Schaaf



Fig. 4. The main building (A) and the place where Dr. Rispens worked (B).

The early work of Dr. Rispens together with Professor J. Hoekstra, his boss during the first years in Rotterdam, was focused on characterizing medium pathogenic and low pathogenic strains of infectious bronchitis virus. Probably around 1960 he initiated studies on duck hepatitis, which was devastating the duck industry in The Netherlands at that time. Duck hepatitis or duck viral hepatitis is a highly lethal disease in young ducklings caused by a virus (duck hepatitis A virus type 1 or DHAV-1), which is classified as *Avihepatovirus* in the *Picornaviridae* group. Dr. Rispens used a local virus isolate, named the Ermelo virus after the location where it was isolated, as a vaccine strain after 52 passages in chicken embryos. Vaccination of breeding flocks provided passive immunity to ducklings which provides protection until age resistance develops. He further showed that primary vaccination followed by a booster vaccination at the beginning of the laying period provide protection for about 9 months. This approach essentially eliminated the disease in The Netherlands. The first results of these studies were reported in 1962 at the XII World's Poultry Congress in Sydney, Australia. More detailed information was published in *Avian Diseases* (2) and this paper is still quoted in the 14th edition of *Diseases in Poultry* published in 2020. The results of these studies also formed the basis for his PhD thesis entitled "De bestrijding van de virushepatitis bij eendekuijken" (The control of duck hepatitis in ducklings). This method replaced the control of the disease by injecting ducklings with antibody-positive serum obtained from ducks at slaughter, a technique which was developed and used in the USA. Dr. Daniel Gaudry met Dr. Rispens in 1969 to discuss the production and use of the DV vaccine, a meeting that resulted in a friendship and collaboration until Dr. Rispens passed away. Dr. Rispens provided the vaccine strain to the Merieux Institute in the late 1960's. The vaccine was produced by Merieux and used in France until 2018. The likely reason to end the production was that France changed to produce mostly Muscovy ducks, which are resistant to DHAV-1 (Dr. Daniel Gaudry, personal communication, 2025).

Almost directly after defending his PhD, Dr. Rispens and his family went for a sabbatical leave to the Avian Disease and Oncology Laboratory in East-Lansing, Michigan. During this period (October 1966 – October 1967), Dr. Rispens focused on the development of a test system to detect avian leukosis viruses (ALV). For this purpose, he developed cloned cell preparations transformed by defective Rous sarcoma virus (RSV), which are unable to produce infectious virus, hence the name "Non-Producer" (NP) cells. When these cells are infected with ALV, infectious RSV is released into the supernatant. The presence of infectious RSV can be detected by inoculated of C/O chicken embryo fibroblasts forming foci of transformed cells or by pock formation on CAMs of C/O embryos. The results of the development of the NP test were published in *Avian Diseases* (3). Although the NP test has been replaced by new assays, it was successfully used in The Netherlands to eliminate ALV in several flocks. To quote Goossen van den Bosch who was one of the owners of a hatchery in the Netherlands: "*In the early 1970's, the hatchery was importing Hy-line grandparents from the USA. The 934^E line had problems with leukosis. Talking with Bart about the problem, he offered to test pure lines from Hy-line using the NP test. Several shipments of eggs, identified with the hen number, were received from the USA. Individual eggs were tested and if positive, the hen was euthanized solving the leukosis problem.*" During one of the meetings Goossen had an interesting discussion with Dr. Rispens. To quote Goossen: "*You (Rispens) do very interesting work.*" The response from Bart was: "*That appears so, but my work is 99% transpiration and only 1% inspiration.*" Dr. Rispens then showed Goossen a small room with a camping bed behind his office with the statement "*I worked here during the weekend with only a few hours of sleep because I had to evaluate a lot of histology slides.*" This was typical for Dr. Rispens, who was driven by science.

During his sabbatical year, Dr. Rispens became familiar with the research on Marek's disease (MD) at ADOL. Although he was not directly involved with the many projects on MD, including the development of the HVT vaccine, he contributed indirectly to the success of the HVT vaccine. Dr. Rispens needed duck embryo fibroblasts (DEF) for the development of the NP cells (3). He convinced Dr. John Solomon, working with Dr. Witter, to use DEF cells for the isolation of the FC126 isolate of HVT, because the DEF grew much better than the chicken embryo fibroblasts (4). On his return to The Netherlands in October 1967, Dr. Rispens returned to the CVI with a strong interest and ideas to start working on MD. Research and development of a vaccine was desperately needed with up to 60% mortality in some flocks in The Netherlands. Under pressure from poultry producers the Production Board for Poultry and Eggs approached the Dutch Organization for Applied Scientific Research (TNO) and CVI in 1964 to start a project on control of avian leukosis, which included MD. Dr. Rispens from CVI and Dr. Henk J.L. Maas from TNO were appointed as project leaders for the CVI and TNO teams, respectively. After returning from his sabbatical year, Dr. Rispens started to isolate pathogenic strains of MD virus (MDV) and was able to reproduce the disease. The observation by Maas that some parts of The Netherlands had poultry farms without the disease but that antibodies to MDV were present in these flocks led Dr. Rispens to isolate strains from these flocks. In preliminary experiments, these strains showed to be of low pathogenicity and more importantly chicks injected with these low pathogenicity strains were protected against challenge with pathogenic strains (5). When Dr. Rispens inoculated lymphocytes from his Line 7₁ flock he isolated a strain that would become the "Rispens" vaccine. Fig. 5 shows two pages of his notebook with the observations on the isolation of the virus from hen number 988.

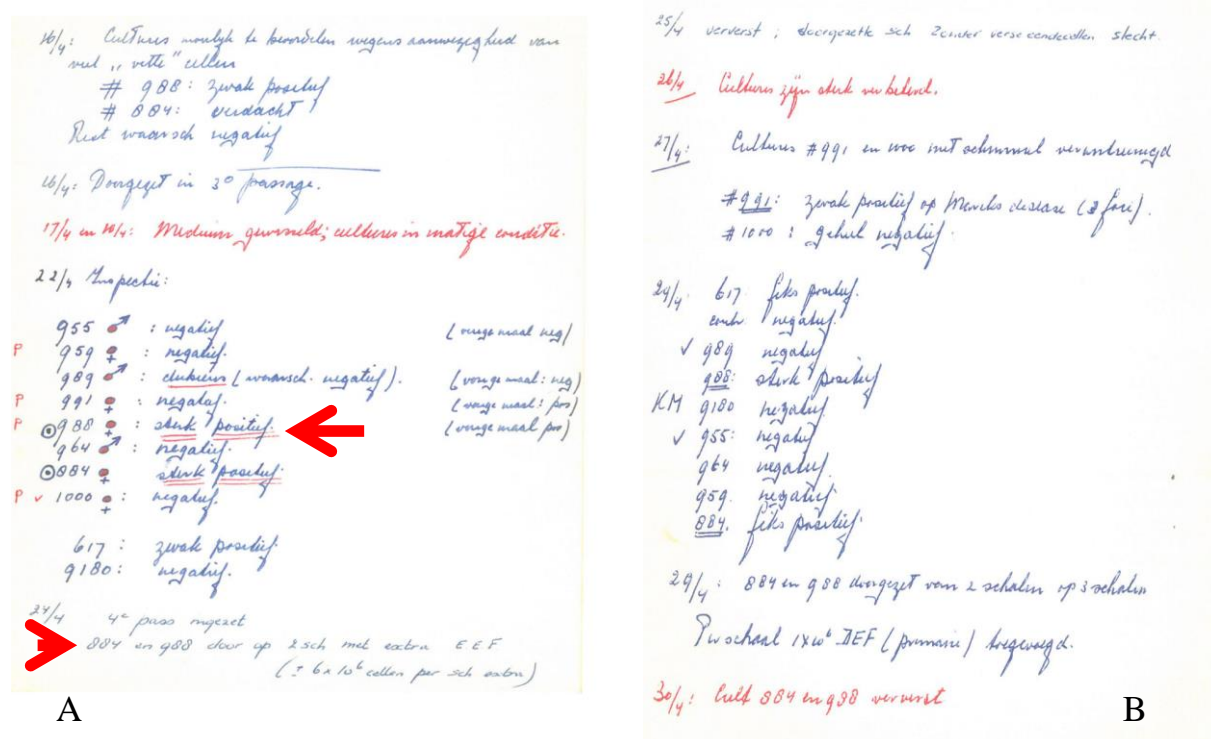


Fig. 5. Isolation of CVI-988 (red arrow) (A) and subsequent passage (B).

After the first laboratory experiments showing that CV988 was able to protect against challenge, some limited field trails were performed in the first 6 months of 1970 vaccinating about 160,000 one-day-old chickens with excellent results. Dr. Rispens participated in vaccinating chicks at the hatcheries! When these results became known the poultry industry started to pressure Dr. Rispens and Maas to start large-scale vaccination procedures. Drs. Rispens and Maas were reluctant to do this because there were still only limited data available without statistical analysis. However, after the Dutch Government provided official support, large scale field trials were conducted. Between August 1970 and April 1971 over 4.5 million chicks were vaccinated providing statistical evidence that CVI-988 was highly effective in protecting chickens against MD. Detailed information on the developments of CVI-988 can be found in several publications (4,6,7). The national vaccination campaign was started, and chicks were vaccinated in a central location (The Institute for Poultry Health in Doorn, which does not longer exist) (Fig. 6).



Fig. 6. The team working on the national vaccination campaign against Marek's disease. From left to right: N. Mastenbroek, B.H. Rispens, W.H. Smits, S.D. Blanksma, J.A.H.C Naber and the vaccination crew. Nel Mastenbroek was a senior technician with Dr. Rispens, Smits was the Director of Institute for Poultry Health

Three Dutch vaccine companies (Laboratory Dr. de Zeeuw (acquired by Intervet in 1988 and now MSD), Philips-Duphar (now Boehringer Ingelheim) and Intervet received the vaccine free of charge and were instrumental in providing the vaccine for the large field trial. In addition, IFFA-Merieux received CVI-988 in 1973 and Lohman Animal Health (LAH) in 1972 free of charge. Dr. Ruud Hein mentioned in an Intervet brochure (8) that CVI-988 was produced as "Rismavac" Nobilis. Dr. Hein expressed some concern that CVI988 was not attenuated and because its spreads horizontally could become virulent.

Yet, notwithstanding the excellent results in The Netherlands the vaccine was not easily accepted elsewhere in the world because high doses of the vaccine could cause some minor MD lesions in genetically susceptible SPF chickens. Goossen van den Bosch was present at a meeting of the Poultry Veterinary Study Group (PVSG) in the EU in Maidenhead (UK) in May 1973, where Rispens presented his work on CVI-988. He was questioned rather harshly about the safety of his vaccine. His response was following Goossen and freely translated by KAS: *"You catch criminals with criminals! MDV is really a hardy criminal, which you can not control with soft measures."* There was also concern about the safety of the vaccine for humans because the disease Dr. Rispens had in 1970, and that caused his death in 1973, was cancer in one of his kidneys. Typical for Dr. Rispens, he examined the histology slides of his tumor and came to the correct conclusion that it was not Marek's disease. Drs. Rispens and Maas arrived in a rather old car at the meeting in Maidenhead, which led to jokes like *"If you developed such a good vaccine, you must be able to*

buy a new car” to which he responded with “*Others received the financial gains of my vaccines, while I have the smell of poverty.*” This was again typical for Dr. Rispens: Because the funding came from the Dutch Government, the product ought to be freely available to the Dutch poultry industry. The world-wide acceptance of CVI-988 took some time and is described in more detail elsewhere (4,7). To quote Goossen van den Bosch once more: “*During a subsequent meeting of the PVSG Dr. Vielitz mentioned that HVT was the best vaccine and that the Rispens vaccine was very dangerous. A few years later Germany experienced major MD vaccination breaks and started to use CVI-988. Vielitz mentioned at the end of the trials with CVI-988: I hate to admit, but Rispens has done a wonderful job.*”

Dr. Gaudry mentioned another characteristic typical of Dr. Rispens: his willingness to share his knowledge of cell culture techniques and virology. To quote Dr. Gaudry: “*When Dr. Burmester presented the results with the HVT vaccine at the 1969 WVPA congress in Belgrade, I contacted him like everyone else in the vaccine industry to see how I could get the virus. Burmester invited me to his laboratory for two six-week visits to learn how to grow HVT, where I worked with Dr. Bill Okazaki. However, when I came back to Merieux, I had trouble growing HVT. Bart invited me to his laboratory to help solve the problem. I took all cell culture media components with me and in a two-week period we learned that the medium I was using was not as good as the medium used by Bart. In addition, I learned that there was also a problem with the incubator in Lyon. During my time in Bart’s laboratory, I learned about the potential interest of CVI-988 and how to grow this virus.*” As mentioned above, Merieux received CVI988 in November 1973, when Dr. Bool shipped five vials of the 28th passage of CVI988 (Gaudry, personal communication). CVI-988 was finally introduced in the USA in 1994 (reviewed in 4).

Dr. Rispens had a strong personality, would fight hard for his team, and did not accept nonsense stories. This would cause sometimes conflicts with his superiors. Dr. Maas mentioned the following story: “*Dr. J. Hoekstra, officially the supervisor of Rispens, had written an article about MD vaccination through the feather follicles prior to the existence of any MD vaccine. During the coffee break, the director of CVI, Dr. van W., asked Rispens what he thought about this article. Rispens clearly thought that the article was worthless. The director ordered him to write the critique in an article, which Rispens refused to do. This was followed by a written order from the Director that the critique needed to be presented within 14 days. When that was not done, the director refused to provide Rispens with tissue culture dishes. Fortunately, I (Maas), working for TNO and in a different location, was able to provide the dishes to Rispens.*” Leo Hertog joined Dr. Rispens as a technician in 1967 and worked with him until 1973. He describes Dr. Rispens as follows: “*He was a very friendly man, and I could work well with him. He was great supervisor for me and the other technicians. Dr. Rispens would work with us at the bench and would join for weekend chores.*” On the other hand, as mentioned before Dr. Rispens did not accept nonsense stories. To quote Leo “*We shared a centrifuge with another scientist who was often moody, and he told me to wait to use the centrifuge, When Dr. Rispens learned about this, he told his colleague in strong words that this was not acceptable.*” When Leo’s son was born Dr. Rispens came to the hospital with a large bouquet of flowers, which surprised his wife! One final quote from Leo “*I have many good memories about my time that I was able to work in research projects under the supervision of an inspiring man, which unfortunately ended way to soon.*”

The recognition of Dr. Rispens. In 1971, the College of Veterinary Medicine in Utrecht awarded Dr. Rispens the prestigious Schimmel-Viruly Award, which is presented every five years to a Dutch researcher who has contributed most to the enhancement of veterinary science.

The Dutch poultry industry clearly profited early on from the research done by Dr. Rispens. The control of duck virus hepatitis saved the duck industry in The Netherlands and elsewhere. The development and subsequent use in The Netherlands of the NP test reduced the incidence of ALV significantly in the period 1969-1973. The development of the MD CVI-988 vaccine has been a major contribution to the control of MD. Especially since the introduction in the USA in 1994 (4,7), the Rispens vaccine is used world-wide as a single, bivalent, or trivalent vaccine. In recognition of these important achievements, the Dutch poultry industry provided Bart and Will Rispens with an all cost paid visit to East-Lansing and Mexico City where Dr. Rispens was able to participate in the 19th World Veterinary Congress (August 16-21, 1971).

In 2013, Dr. Rispens was inducted in the inaugural class of the Hall of Honour of the World Veterinary Poultry Association. His work was also described in the Merial Biographies Leaders and Legends series 6:14-15, 2010, which can be found in the biography section of the History of Avian Medicine section of the AAAP website.

In 2016, Dr. Rispens was featured on the front cover of Avian Diseases volume 60, 4th issue. The inside cover story highlighted his work on duck hepatitis, the development of NP cell and most importantly the development of the Rispens vaccine.

The Dr. Bart Rispens Memorial Award Fund.

Dr. Maas took the initiative in 1973 to establish the Dr. Bart Rispens Memorial Award Fund with two goals in mind. The first one was to honor Dr. Rispens through the Research Award. The second goal was to establish a Trust Fund for the education of his two children Jan Albert and Babs. Gifts from industry sources, other organizations, and friends of Dr. Rispens provided the funding. A Board of Trustees was established with Dr. Burmester as Chairman and Dr. Maas as secretary. In 1987, Dr. Schat replaced Dr. Burmester as chair of the Board of Trustees, while Dr. Jan-Kees van den Wijngaard and later Dr. Guus Koch served as secretary. During the 1990's the Board of Trustee distributed the remaining funds in the Trust Fund to Jan Albert and Babs. The Research award was, and still is, based on the best paper published in Avian Pathology during the two calendar years preceding the World Veterinary Poultry Association (WVPA) congress. The Trust Fund was officially ended in 2007 and the responsibility for the research award was transferred to the WVPA. The award consisting of a medallion (Fig. 7), a certificate and a monetary award was presented for the first time in 1977. The list of all awardees can be found at the website of the WVPA (<https://wvpa.info/awards/>).

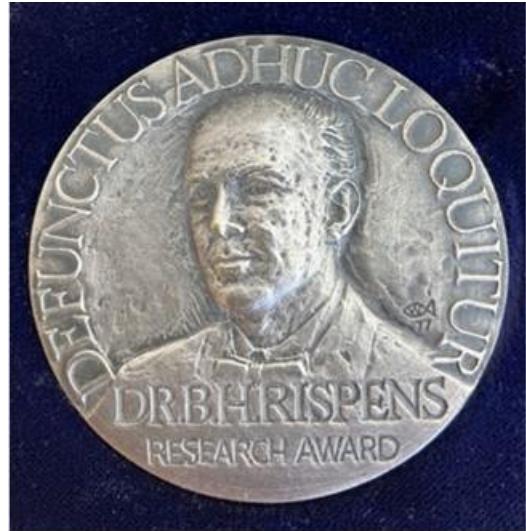


Fig. 7. The Dr. Bart Rispens Award Medallion for the best publication in two volumes of Avian Pathology

Personal Reflections of K.A Schat. I met Dr. Rispens for the first time in December 1969 when the poultry rotation group visited CVI and Dr. Rispens gave a presentation on his work with CVI-988 to the veterinary students and others. At that time, I did not have a specific interest in poultry diseases, but I was fascinated by the research because he was an excellent speaker. The second time was when I interviewed for a position with the Dutch International Technical Assistance Program to set up a Marek's disease program in Mexico (see my autobiography for details). When I was selected for the program, Dr. Rispens became my first mentor in MD research. The 5 months of training under the guidance of Dr. Rispens formed the basis for starting the project in Mexico. I will never forget the day that I joined him and the vaccination crew to vaccinate chicks at one of the hatcheries. Nor will I forget the day that he took me to Intervet (still Nobilis at the time) in Boxmeer and introduced me there to Professor Peter Biggs.



Fig. 9. Banquet at the World Veterinary Congress Mexico City, 1971. From left to right: Mrs. Burmester, Ton Schat, Gerda Schat-van der Woude, Bart and Will Rispens, Ben Burmester, Gosse Bijlenga.

During the visit of Bart and Will to East-Lansing I was able to join them for two weeks. Bart, Will and I stayed the first week with Graham and Nancy Purchase and the second week we stayed in the house of Dr. Burmester who was on vacation. During that week, Bart and I worked on the revisions of the two manuscripts describing CVI-998 (reference 6). During their time in Mexico, Bart and Will Rispens stayed with Gerda (my ex-spouse) and me. This was a wonderful time to show Bart and Will around in Mexico City and the Instituto Nacional de Investigaciones Pecuarias, where I was stationed. One of the highlights of their visit was the banquet during 19th World Veterinary Congress (Fig. 9).

During my home leave in 1973 I joined Bart in the new facilities in Lelystad for 3 months, of course not knowing that he would pass away later in that year. The support of Bart in getting the position in Mexico has been of crucial importance for my career in avian disease research.

References and acknowledgements:

1. Maas, H.J.L. In memoriam: Dr. Bart Helmich Rispens. *Tijdschr. Diergeneesk.*, 99:639-640, 1974.
2. Rispens, B.H. *Avian Dis.* 13:417-426, 1969.
3. Rispens, B.H., et al. *Avian Dis.* 14:738-751, 1970.
4. Schat, KA. *Avian Dis.* 60:715-724, 2016.
5. Rispens, B.H., et al. *Br Vet J.* 125:445-453, 1969.
6. Rispens, B.H et al. *Avian Dis*, 16:108-125 and 126-138, 1972.



Fig 8. Dr. W. (Bill) Okazaki, Dr. Bart H. Rispens and DVM Karel A. (Ton) Schat in front of the Regional Poultry Research Laboratory in East-Lansing, MI, USA in the summer of 1971. Photo collection K.A. Schat.

7. Bool, P.H. In: Strictly scientific and practical sense. A century of the Central Veterinary Institute in The Netherlands 1904-20024. P. Verhoef, J.M. van Leeuwen and P.H. Bool, eds. Erasmus Publishing, Rotterdam. Pp 197-199. 2007.

8. Hein, R.G. Marek's disease and the control of Marek's disease with freeze-dried Marek vaccine Nobilis. Intervet International, Boxmeer, Holland. pp 1-23, 1972.

The authors of the biography thank Dr. Henk Maas (deceased), Dr. Daniel Gaudry, Dr. Goossen van der Bosch, Leo Hertog for personal communications, which added valuable information. Dr. Ruud Hein provided reference 8. Dr. Guus Koch for critically reviewing the document.

Photo credits: Fig. 1-3, and the photo on page 1: Jan Albert Rispens, Fig. 4-6 were previously published in reference 4. Fig. 7-9 are in the personal collection of K.A. Schat.

Biography solicited by the Committee on the History of Avian Medicine, American Association of Avian Pathologists.

Additional biographical materials may be available from the AAAP Historical Archives located at Iowa State University. Contact information is as follows:

Special Collections Dept. & University Archives

403 Parks Library

Iowa State University

Ames, IA 50011-2140

Phone: (515) 294-6648

Fax: (515) 294-5525

WWW: <http://www.lib.iastate.edu/spcl/index.html>