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# On the Origins of the Druckrey-Küpfmüller Papers (1948-1949): Dose-Effect Relations in Carcinogenic Substances #\*

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Summary:

Theoretical knowledge about the relationship between drug dosage and tissue response in pharmacology and toxicology in general, and concerning the action of carcinogenic substances in particular, largely dates back to two papers by Hermann Druckrey and Karl Küpfmüller, published in 1948 and 1949, respectively. The definition of cumulative poisons and the first proof of the irreversibility of carcinogenic effects had an extraordinary impact on cancer research. The story of how these papers came to be written is remarkable for several reasons. First, an interdisciplinary approach resulted in a landmark interpretation of data regarding the quantitative analysis of cancer development. Second, an intensive collaboration developed between Druckrey, a cancer researcher, and Küpfmüller, a mathematically adept electrical and communications engineer. Third, during their temporary "full-time co-operation", both researchers were in an allied internment camp. Thus, their fundamental scientific achievement ultimately resulted from the fulfilment of three conditions of innovation, i. e. compatible visions of the co-operating scientists, interdisciplinary links, and chance.

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#### Key words:

Druckrey, Hermann – Küpfmüller, Karl – Heubner, Wolfgang – Butenandt, Adolf – cancer development – chemical carcinogenesis – dose-response data – German Research Foundation – pharmacology – communications technology – National Socialism – allied internment camp

"Of that which man ought to be, even the best of us know little that can be relied on. Of that which he is, we can learn something from everybody." Georg Christoph Lichtenberg (1742-1799)

#### Introduction

Anyone who attempts to look more closely at the circumstances surrounding the accomplishments of German researchers during the era of National Socialism or the immediate postwar period, will move through a minefield. Time and again, the "unholy alliance" between the relevant researcher and the NS regime can reveal itself providing cause for reflection. This will be presented in the following using the example of groundbreaking interdisciplinary research.

In 1948, an article by Hermann Druckrey (1904-1994) and Karl Küpfmüller (1897-1977) titled "Quantitative Analysis of the Origins of Cancer" appeared in the *Zeitschrift für Naturforschung* [Journal of Natural Science].<sup>1</sup> One year later, a publication by the same authors appeared titled, *Dose-Effect Relations. Contributions to Theoretical Pharmacology,* which was reprinted in its original form in 1985.<sup>2</sup> In the preface, it is described as the "product of a lengthy and close collaboration between a medical professional and a physicist that was made possible through the *external circumstances of the times* [emphasis by VW]."<sup>3</sup> Furthermore, there was an additional joint publication by these two productive researchers on a different topic.<sup>4</sup> Whereby the first study dealt with planning, conducting, and evaluating a large-scale animal experiment concerning the carcinogenic

<sup>&</sup>lt;sup>1</sup> Druckrey and Küpfmüller (1948).

<sup>&</sup>lt;sup>2</sup> Druckrey and Küpfmüller (1949).

<sup>&</sup>lt;sup>3</sup> Ibid. p 514. Küpfmüller was not, however, a physicist, but rather had an electrical engineering background.

<sup>&</sup>lt;sup>4</sup> Druckrey, Küpfmüller and Trappe (1949). This paper was sent to the publisher on March 31, 1949.

effects of a chemical substance (dimethylamino-azobenzene<sup>5</sup>, "butter yellow"), the second study derived general and largely novel principles related to the toxic effects, whereby cancer formation was understood to be a pharmacological process. That these very complex processes follow mathematical rules was first proven through the experiments by Druckrey and Küpfmüller and is still widely accepted today. Druckrey and associates made important contributions related to this topic in the 1950s and 1960s. Based on numerous experiments that produced liver cancer in rats through various types of carcinogens, the relationship between latent time *t* and daily dose *d* was established and presented in the following equation:

 $\log d = \operatorname{const} - n \log t$ 

The equation shows that a straight line is obtained by employing t and d in a double logarithmic net. The slope of the line, n, ("Druckrey *slope*") is specific for each chemical carcinogen and n>1 always applies. The relationship is valid in the liver and other organs including fetal organs, and independent of the species. It describes the effect of one-time and chronic carcinogenic effects.<sup>6</sup>

A fundamental conclusion of the experiments was already clearly formulated in the first paper and then repeatedly confirmed thereafter:

Thus, even with the smallest single dosage, the carcinogenic effect of "butter yellow" remains *irreversible* [emphasis in original] from the beginning of the experiment throughout the entire lifetime and gets added to the effect of later doses without being diminished [...] Because cell division usually occurs at this time, the effects are transferred to the daughter cells.<sup>7</sup>

This fact – the undiminished summation of individual doses due to genotoxic effects – is the cornerstone of our current knowledge of the mechanisms of carcinogenesis. It is of great practical value in estimating the risk of small and very small doses of genotoxic substances in the human environment. Therefore, the historical circumstances that led to the recognition of this fundamental principle deserve our attention.

## A Special Publication

<sup>&</sup>lt;sup>5</sup> Former German nomenclature was benzol.

<sup>&</sup>lt;sup>6</sup> Druckrey (1967).

<sup>&</sup>lt;sup>7</sup> Druckrey and Küpfmüller (1948), p. 259 and 254.

The first publication by Druckrey and Küpfmüller was a milestone in the research on chemical carcinogenesis.<sup>8</sup> Its appearance was unusual alone due to the productive collaboration between a cancer researcher (Druckrey<sup>9</sup>) and an electrical and communication engineer (Küpfmüller<sup>10</sup>). It happened as the result of external circumstances that will be described later. The substantive affinity must have played a decisive role. The interests of both men extended far beyond their narrow specialties. Druckrey had long wanted to attempt a quantitative description of carcinogenesis and had conducted relevant animal experiments. Küpfmüller had been working intensively at that time on his system theory and had apparently considered its applications in biology.<sup>11</sup> In the later years, he successfully completed fundamental research on the electrical simulation of biological processes. Moreover, the personal experience of cancer (Küpfmüller's mother died of stomach cancer at age 52<sup>12</sup>) sensitized him to the topic.

No one could have guessed how modern and forward-looking it was to incorporate electrical and communication engineering into the discussion of cancer formation. The potential inherent in the personal connection could not have been recognized or even be fully realized, however, because the collaboration between Druckrey and Küpfmüller was only temporary. The collaboration was driven largely by a pharmacological perspective and Druckrey's interest focused primarily on Küpfmüller's mathematical and theoretical skills. It was not until decades later that it was proven that living cells and tissues are complex regulatory systems whose precisely balanced condition is maintained by intraand inter-cellular signals. Numerous proteins that interact with one another through modules constitute signal chains with many links that cells use to communicate with their environment. The diverse signal transmission mechanisms of cells resemble, in some ways, the integrated circuits of electronic components. Permanent disruptions in the signal flow, possibly through the mutation of relevant genes, can be the event that triggers cancer. The constitutive activation of signals that are no longer controlled exogenously is a typical transformation mechanism resulting in malignant growth.<sup>13</sup>

The manuscript published in 1948 in the *Zeitschrift für Naturforschung* [Journal of Natural Science] was submitted to the publisher on June 5, 1947. Control and responsibility for the animal experiments was clearly held by Druckrey who, however, was only released from captivity in 1947.<sup>14</sup> Consequently, only the manuscript could have been prepared in 1947. Where and when were the experiments conducted? Who financed them? The published paper provides no clue in this regard. Druckrey used the address of the

<sup>&</sup>lt;sup>8</sup> Miller and Miller (1979), p. 449.

<sup>&</sup>lt;sup>9</sup> See Appendix 1 for a tabular overview of life and works.

<sup>&</sup>lt;sup>10</sup> See Appendix 2 for a tabular overview of life and works.

<sup>&</sup>lt;sup>11</sup> Küpfmüller published a study on a biological issue in 1921.

<sup>&</sup>lt;sup>12</sup> BArch (formerly BDC) [TN: BArch stands for Federal Archives Berlin-Lichterfelde and BDC for Berlin Document Center] RS D391, 1013.

<sup>&</sup>lt;sup>13</sup> For a recent summary, see Vogelstein and Kinzler (2004).

<sup>&</sup>lt;sup>14</sup> Hermann Druckrey. In: Munzinger Achives, 1989.

Department of Surgery at Freiburg University Hospital. However, he was not hired there until 1948. Küpfmüller only provided a private address in Stuttgart. It is clear that private citizens alone without financial support could not have managed such a large-scale (more than 740 animals) and lengthy (more than 2 years) experimental program that required a properly equipped animal lab and qualified staff. Even today, silence regarding the location and timing of the experiments is cause for reflection among readers. This manner of proceeding was uncommon even then, although a peer-review process in its current form today did not yet exist. The comment in the footnote, "Due to time-related factors, the paper could only now be published" is not clear. It could mean that printing took unusually long or that a publication-ready manuscript could not be accepted for publication quickly due to the end of the war.

It would take extensive research to clarify the many unanswered questions that are directly connected to the emergence of this paper. For this effort, an in-depth study of the biographies of both authors, particularly for the years 1942 to 1948, was unavoidable. The results are presented first briefly and then in greater detail below.

The experiments were conducted at the Pharmacological Institute of the Friedrich-Wilhelms University of Berlin up until spring 1943 (Director: Prof. W. Heubner). Druckrey was forced to leave this Institute after a dispute. Thereafter, the experiments were carried out to completion at various locations. The work was supported by the German Research Foundation (DFG) primarily in the years 1941 to 1944 under the title, "Hormones and Cancer."<sup>15</sup>

Due to their involvement with National Socialism, but independent of one another, both authors were placed in an internment camp by the Allied Military Government. In one such camp, Druckrey and Küpfmüller met and used the opportunity that was apparently available to engage in intensive discussions regarding scientific issues from the perspective of their very different areas of specialization. The "prolonged and close collaboration" took place during their joint internment which led to the publication mentioned at the outset. Druckrey hinted at this in 1981 when stating his position in *Citation Classic*:

After the war, an otherwise precarious situation permitted a unique full-time cooperation with the electrophysicist K. Küpfmuller in elaborating the theoretical foundations of pharmacokinetics and ergokinetics both to understand the earlier results and to systematically plan new experiments.<sup>16</sup>

<sup>&</sup>lt;sup>15</sup> Funding was available to Druckrey intermittently from the Reich Ministry of the Interior (Druckrey [1943], p. 532).

<sup>&</sup>lt;sup>16</sup> Citation Classic (1981).

## The Participating Researchers and Their Contributions

## Hermann Druckrey<sup>17</sup>

When Druckrey was 19 years old, his father, a practicing pharmacist, died of cancer at the age of 51. It is possible that his decision to join the Viking-League/Ehrhardt-Brigade <sup>18</sup> one year later had to do with this loss. In any case, he was an active National Socialist from relatively early on.<sup>19</sup> His career prospects were also promising from relatively early on and would not have required an alliance with the NS-politics. After completing medical school, he sharpened his scientific profile through a 6-month residence in a department in which he worked with Adolf Butenandt (1903-1995) of like age and repeated work-related visits to the Zoological Station in Naples. Approximately beginning in 1933, Druckrey began to devote himself to cancer research. In the Pharmacological Institute of the Charité Berlin, they found well-intended support through the director of the Institute, Prof. Wolfgang Heubner (1877-1957).<sup>20</sup> A Lecturer in 1936 who went on to be promoted to Adjunct Professor in 1942, Druckrey, was one of the researchers supported by large sums from the DFG or the Reich Research Council from 1937 to 1944.<sup>21</sup> Beginning in 1936, Norbert Brock and Hans Herken worked in his work group as research fellows.<sup>22</sup>

In addition to his research and teaching activities, Druckrey held important positions of authority in the early years. Beginning in 1936, he was part of the board of directors of the German Pharmacological Association and part of the Scientific Committee of the Reich Committee for Cancer Research beginning in 1938. He was politically influential as representative of the NS-Lecturer Association in the Department of Medicine at the

<sup>18</sup> A free corps named after its leader, Hermann Ehrhardt (1881-1971); an elite military formation that conducted anti-insurgency actions during the Weimar Republic. Successor organizations were the Viking-League and the organization-Consul. Under SS control after 1933, "the spirit of this force was already in 1920 the spirit of the future Waffen-SS." (Haffner [2002], p. 178).

<sup>&</sup>lt;sup>17</sup> For life and Works, see Appendix 1.

<sup>&</sup>lt;sup>19</sup> A collection of information that will be presented in the following can be found in the files on the denazification of Druckrey. The procedure ended on April 8, 1948. The files are kept in the Central Archives in Dusseldorf (HStAD NW 1002-G, No. 45495) and were made available through a staff member of the Archives, Dr. Matthias Meusch.

On January 30, 1948, Professor W. Heubner wrote to the denazification committee that Druckrey was "a deeply convinced Nazi, not out of opportunism, but out of sincere patriotism; he ardently believed that this ideology and party would be a blessing to his country."

<sup>&</sup>lt;sup>20</sup> For more information, see Kneer (1989). In the text, Druckrey is not mentioned.

<sup>&</sup>lt;sup>21</sup> Compare to Deichmann (2001), Tab. 5.5, p. 232. Regarding the tumor research program of the DFG and the Reich Research Council in the years 1933-1945, see Steinwachs (2000) and Moser (2005).

<sup>&</sup>lt;sup>22</sup> Brock (born 1912) later became famous world-wide through the development of cancer therapies (Cyclophosphamide, Ifosfamide) in the ASTA-Works. Herken (1912-2003) followed Heubner 1953-1983 to the Department of Pharmacology of the Free University of Berlin. He is recognized as one of the founders of biochemical pharmacology.

University of Berlin. In Berlin-Brandenburg, he was the Head SA-Physician during the war and was, among other things, responsible for paramedic training of SA teams [*TN*: SA refers to "Sturmabteilung" which was the storm troop division of the NSDAP].

Druckrey's appointment at the Berlin Pharmacological Institute ended in the spring of 1943. At different times, he provided different reasons: he left of his own accord (per 1942 and 1944<sup>23</sup>); he was drafted to the war front (per 1947<sup>24</sup>); or he was forced out of the Institute by a group of persons currently living in the Russian section of Berlin (1948<sup>25</sup>). The first reason (as already noted by Deichmann<sup>26</sup>) does not seem plausible because Druckrey was able to work under very good conditions and would not have endangered his important yet nascent findings in any way at that time. Being drafted into the military would not have required his resignation from the university. The third reason was likely a delayed attempt at justification during the emerging Cold War period.

A reconstruction of the events that led to his resignation is based on reports by witnesses<sup>27</sup> made as part of the delayed denazification proceedings in 1947/48 as sworn testimony and formally recorded.<sup>28</sup> Thereafter, a political conflict smoldered for years between Heubner who did not think much of National Socialism and liked to make this view public, and Druckrey, a young, dynamic National Socialist with a high level of expertise. It evolved into a fight over leadership at the Institute. Heubner reported that, even as an assistant, Druckrey had repeatedly and urgently attempted to get him to join the National Socialist German Workers' Party (NSDAP) and let him know "that he was charged by his party with overseeing the political relations in the Institute."<sup>29</sup> At first, he took it in stride because he appreciated Druckrey's "scientific initiative, work ethic, and intelligence." Druckrey, in contrast, had "dangerously exposed" himself multiple times to the Party on behalf of his superior "and the dismissal of the seasoned and internationally known university instructor could only be avoided"<sup>30</sup> by Heubner making candid statements that endangered both him and the Institute. In November 1942, however, the problems escalated.<sup>31</sup> It came to heated arguments in the presence of witnesses during

<sup>&</sup>lt;sup>23</sup> Druckrey to the University Curator in Berlin, November 30, 1942: BArch R26/III/4901/14565; Druckrey to DFG, November 30, 1942: BAK R73/10787; Druckrey (with Curriculum Vita) to Prof. Rostock, July 1, 1944: BArch (formerly BDC) PK BO 396/1570.

<sup>&</sup>lt;sup>24</sup> Druckrey denazification files, HStAD NW 1002-G, No. 45495.

<sup>&</sup>lt;sup>25</sup> Ibid.

<sup>&</sup>lt;sup>26</sup> Deichmann (2001), p. 346.

<sup>&</sup>lt;sup>27</sup> Lindner and Luellmann (1996) provide an overview on the academic collaborators at Heubner's Institute, p. 23.

<sup>&</sup>lt;sup>28</sup> Druckrey's denazification files (cf. note 24).

<sup>&</sup>lt;sup>29</sup> Prof. Heubner to the denazification committee on January 30, 1948, Druckrey denazification files (cf. note 24).

<sup>&</sup>lt;sup>30</sup> Sworn statement by Prof. G. Orzechowski, March 11, 1948, ibid.

<sup>&</sup>lt;sup>31</sup> See also the description by Deichmann (2001), p. 346.

which Druckrey "seriously insulted" the Director of the Institute<sup>32</sup> and threatened to "slap him for his defeatism, ...although he declined to do so after referring to Prof. Heubner's age."<sup>33</sup> With this, the breach between Heubner and Druckrey became unavoidable. A hearing before the Dean of the Faculty, Prof. Paul Rostock (1892-1956), followed which produced a "formal reconciliation and a notice of termination effective<sup>34</sup> April 1, 1943.<sup>35</sup> Druckrey attempted to use his connections to the Party to have the termination reversed but was not successful.<sup>36</sup>

Druckrey was also not successful in preventing his draft into the war front. With a letter dated March 5, 1943, the university curator lifted Druckrey's temporary exemption from military service.<sup>37</sup> Looking back to 1948, he wrote:

I was then sent to the war front in April 1943, that is, at a time when practically all other researchers and certainly all professors had long since been called back due to the so-called "Osenberg Action."<sup>38</sup> [...] So, back then, I was the only German professor and researcher who worked as a simple military physician in the trenches of the war front.[...] I was called to the front because, for certain party leaders, in particular the 2<sup>nd</sup> Reich Health Leader, Prof. Blome and the Ministerial Director of the Ministry of Culture SS-Group Leader, Prof. Menzel,<sup>39</sup> I stood in their way.<sup>40</sup>

In his role as an NS-Lecturer Association official at the Charité, Druckrey completed a variety of different political certificates. Reflecting back, the pharmacologist, Ludwig Lendle (1899-1969) noted:

Although he did not get a position in this area, he was consulted by the Ministry of Culture and the head of lecturers regarding matters of filling teaching positions in our field. In terms of the positions I am familiar with, he never stood for people with good political credentials

<sup>&</sup>lt;sup>32</sup> Prof. Robert Havemann (1910-1982) to the denazification committee on February 7, 1948, Druckrey denazification files (cf. note 24).

<sup>&</sup>lt;sup>33</sup> Friedrich Jung (1915-1997): obituary for Prof. H. Druckrey. In: Scheler and Oehme (2002), p. 172f. See also note 35.

<sup>&</sup>lt;sup>34</sup> Heubner and Druckrey had stated these dates in their correspondence with the university curator on December 4, 1942 and to the DFG on November 30, 1942.

<sup>&</sup>lt;sup>35</sup> Sworn testimony from Dr. F. Bergmann, January 31, 1948. He also testified that Druckrey threatened to physically harm Heubner. Druckrey's denazification files (cf. note 24).

<sup>&</sup>lt;sup>36</sup> Druckrey's denazification files (cf. note 24).

<sup>&</sup>lt;sup>37</sup> University curator to the Wehrkreis command in Berlin VI, March 5, 1943, BArch R26/III, 4901/14565.

<sup>&</sup>lt;sup>38</sup> Prof. Werner Osenberg (1900-1974) worked in the Reich Research Council in charge of planning. In 1944, he initiated the return of numerous professionals from the war into research (Federspiel [2002]; Klee [2003]).

<sup>&</sup>lt;sup>39</sup> Referred to here is Prof. Rudolf Mentzel (1900-1987), SS-Brigade Leader, and beginning in 1939, the Ministerial Director and Agency Head in the Reich Ministry of Science, Education, and Training and simultaneously president of the DFG (1936-1945), and formerly a completely unknown Chemist in his field (Deichmann [2001], p. 217 f.).

<sup>&</sup>lt;sup>40</sup> Druckrey denazification files (cf. note 24).

but poor expertise. On multiple occasions, he expressed very strong negative criticism against such potential placement errors.  $^{\rm 41}$ 

Prof. Kurt Blome (1884-1969) "whose expertise had been called into question multiple times"<sup>42</sup> was also sharply criticized by Druckrey for factually inaccurate representations of cancer issues. Naturally, rivalries within the Reich Research Council to be the thought leader in the area of cancer research certainly played a role. Shortly after Druckrey's conscription on April 30, 1943, Blome was named Plenipotentiary for cancer research by the president of the Reich Research Council, Hermann Goering (1893-1946). What Druckrey could not know (and was also not meant to know): Blome's appointment also served as a cover for highly secret plans. For "under the title of cancer research" was also a 'secret' research contract for the defense against biological warfare.<sup>43</sup> Up until the end of the war, all research related to biological weapons was declared by Blome to be cancer research. It is plausible that Blome would want to keep Druckrey, who was known for his critical inquiries, at a distance from these secret plans. Conscription into the military may well have presented itself as a solution.

However, there may be another explanation for the events in the winter of 1942/43. It is possible that at this time, Druckrey already knew that the Reich physician-SS and Police, Prof. Ernst-Robert Grawitz (1899-1945) was planning a pharmacological institute and he was being considered as director of the institute. For this position, it may have been viewed as required that the incumbent have a period of service with the SS and Police troops and possibly also to have served on the front. In this case, it would have been clear to Druckrey that he would have to soon leave the University of Berlin and that he would be called to the front for some time. He could then risk the break with Heubner or even deliberately bring it about to create a legend. <sup>44</sup> Moreover, Grawitz and Mentzel agreed that Grawitz's budget requirements (Institution founding, "management positions")

[...] to the extent that they [...] are directed towards the development of scientific research opportunities [...] will deal *exclusively* [emphasis added by VW] with such matters that can only be conducted with the materials (prisoners) that are available to the Waffen-SS and thus cannot be taken over by any other research facility.<sup>45</sup>

<sup>&</sup>lt;sup>41</sup> Prof. Lendle to the Denazification Committee, February 11, 1948, ibid.

<sup>&</sup>lt;sup>42</sup> Geissler (1998), p. 83.

<sup>&</sup>lt;sup>43</sup> Blome, cited in Geissler (1998), p. 57.

<sup>&</sup>lt;sup>44</sup> One basis for this speculation can be found in the correspondence between Grawitz and Mentzel in February 1943 (BArch R26/III 531) and in the heated argument with Heubner in the Druckrey denazification files (cf. note 24).

<sup>&</sup>lt;sup>45</sup> Mentzel, March 25, 1943 to the Reich Ministry of Finance, BArch R26/III 531.

Druckrey's deployment to the front occurred in April 1943<sup>46</sup> and lasted approximately one year. He was then detailed per priority command from the Reich Physician-SS and Police to Vienna on June 3, 1944 to set up the newly founded Pharmacological Institute of the Police<sup>47</sup> that "formally operated outside of the [Vienna Medical] School, but was, in fact, closely tied to it in many ways as well as to the central SS institutions."<sup>48</sup> Apparently, the institute's founding occurred in connection with events in which "the department was promised to be transformed into the driving force of the National Socialist race and annihilation policy."<sup>49</sup> How close it came to carrying out these plans before the end of the war, even with constant support from SS authorities<sup>50</sup> is not known. The Institute was moved to Thumersbach [Austria] on Lake Zell on March 1945. It was there that Druckrey was arrested by the Counter Intelligence Corps (CIC) of the United States Army on May 16, 1945.<sup>51</sup>

## "Hormones and Cancer:" Druckrey's DFG Project

Druckrey's experiments had been generously supported by the German Research Foundation (DFG) since 1937.<sup>52</sup> Because of this, he was able to employ several research fellows and technical staff. A variety of different projects were captured under the title "Hormones and Cancer. (Record number Dr 2/06). Experiments on carcinogenic substances represented just one research direction. Experiments with butter yellow were first mentioned in a report dated March 7, 1938 to the DFG later published in 1940<sup>53</sup> confirming the results of Japanese authors. In another report dated February 25, 1941, it was stated:

Plans for the experiments in the coming year naturally have to take the war situation into consideration. Specifically, experiments that can be conducted even in the absence of research fellows<sup>54</sup> and with the assistance of technical

<sup>&</sup>lt;sup>46</sup> On June 29, 1943, Druckrey wrote to Butenandt, "How nice it is to serve as a 'soldier among soldiers' on the front, cited in Proctor (2000b), p. 12.

<sup>&</sup>lt;sup>47</sup> Letter from the Reichsfuehrer-SS and the Reich Physician and Police dated November 7, 1944 to the Chief of the Ordnungspolizei. (*TN:* Order Police *or* ORPO): "In accordance with the above referenced special order, effective 10/10/1944, the Director of Medical Services was made head of the pharmacological-toxicological research center in the Vienna Police Hospital and called it 'the Pharmacological Institute of the Police.' The head of the Institute is the Chief Staff Surgeon of the Reserve Police, Prof. Druckrey. The Institute is available upon request to answer any pharmacological or toxicological questions. [signature] Grawitz" BArch (formerly BDC) DS B28/2018.

<sup>&</sup>lt;sup>48</sup> Hubenstorf (1989), p. 262.

<sup>&</sup>lt;sup>49</sup> Ibid.

<sup>&</sup>lt;sup>50</sup> Letter from Druckrey to the Ordnumgspolizei Headquarters in Biesenthal/Berlin dated October 16, 1944, BArch (formerly BDC), DS B28, Bl. 2050; see also Hubenstorf (1989): p. 262.

<sup>&</sup>lt;sup>51</sup> A records collection of the camp detailed below and the prisoner records of the Hammelburg internment camp may be found in the Bavarian Main State Archive in Munich. All information regarding this is from Dr. Christoph Bachmann, M.A., Board of Archives, on August 13, August 27, and September 9, 2004.

<sup>&</sup>lt;sup>52</sup> DFG-files H. Druckrey, BAK R73/10787.

<sup>&</sup>lt;sup>53</sup> Brock et al. (1940).

<sup>&</sup>lt;sup>54</sup> Reference here is being made to Dr. Brock who was drafted into the military in the summer of 1939.

staff should be given priority. These are the animal experiments that are relatively expensive.[...] This will require animal materials in the amount of approximately 1500 rats.

On May 12, 1942, the Reich Research Council provided Druckrey the large sum of 14,000 Reichmark. The assumption that Druckrey had already intended to use this large number of rats for experiments with butter yellow at that time is confirmed in statements made in his report dated November 30, 1942: "Furthermore, my quantitative experiments on the carcinogenic effects of dimethylamino-azobenzene that relied on the animal material of almost 800 rats are now coming to a conclusion." The main findings had already been reported in 1948 in the *Zeitschrift für Naturforschung* [Journal of Natural Science] although the experiments were still being conducted. When Druckrey left the Pharmacological Institute in April 1943, it was then necessary "to completely remove the entire material [particularly the lab animals] as soon as possible from the Pharmacological Institute." The remaining pure breed rats and mice [...] were sent to Prof. BUTENANDT in the Kaiser Wilhelm Institute in Dahlem and, with permission from the DFG, Druckrey coordinated that:

All lab animals that were taking part in long-term experiments would continue to be taken care of by Ms. [Hedwig] SEIDE, hitherto my technical assistant, specifically as my representative and under the direction of Dr. [Rudolf] VIERTHALER, Lecturer, who made the requisite space and facilities available in the Bacteriological Department of the Military Physician Academy [Berlin, 35 Scharnhorst St.] that is under his direction. Here too there will be a close connection with Prof. BUTENANDT. The German Research Council's jurisdiction is hereby retained.<sup>55</sup>

To Druckrey, who at this point in time was already in the military, the Reich Research Council (Reichforschungsrat, RFR) approved on May 7, 1943 an additional 7,000 Reichmark expressly to pay for, among other things, support staff to ensure the continuation of the experiments. As part of a larger effort to prepare for war, this was to overlap and supplement research institutions created by DFG. In October 1943, Seide and Vierthaler received the order to transfer to Giessen. From there, Vierthaler requested that DFG increase the research grant by an additional 1,000 Reichmark on February 7, 1944. The RFR promptly complied with the request. After Druckrey returned from the front and became operational in Vienna, Druckrey received an additional 12,000 Reichmark from the RFR on July 28, 1944 to continue research on what was now known as "Investigations into Carcinogenic Materials." Report writing usually followed a six-month schedule. The final two reports submitted were sent from Berlin to DFG on November 30, 1942 and from Vienna to the director of Medical Services at the beginning of October, 1944.<sup>56</sup>

<sup>&</sup>lt;sup>55</sup> Letter from Druckrey to DFG on April 16, 1943, H. Druckrey's DFG-files (cf. note 52).

<sup>&</sup>lt;sup>56</sup> BArch (formerly BDC) DS B28, 2032.

Based on this information, it is possible to approximately reconstruct the sequence of the quantitative experiments with butter yellow. The experiments started in 1941/42 in the Berlin Pharmacological Institute and also ended there with the doses of 3 to 30 mg per day.<sup>57</sup> This allowed Druckrey to draw his first conclusions already in 1942.<sup>58</sup> A large share of the rats receiving the doses of 0.1 to 1 mg/day<sup>59</sup> was still in the experimental stage when Druckrey had to leave Berlin since the natural death of the animals needed to be awaited. The rats allegedly were transported at least once within Berlin from the Pharmacological Institute to the Military Physician Academy, perhaps even an additional two times from Berlin to Giessen and Giessen to Vienna. In June, 1944, Ms. Seide arrived in Vienna before Druckrey with lab animals and the laboratory inventory.<sup>60</sup> By the end of the war, Druckrey had made the results of all experiments available.

#### Karl Küpfmüller<sup>61</sup>

Both before and after the Second World War, Küpfmüller was viewed as one of the pioneers of general electrical and communication engineering. Due to his high profile publications and through the support of Karl Wilhelm Wagner (1883-1953) from early on, he was promoted to full professor for electrical engineering at the Danzig Institute of Technology at the age of only 31 although he had no formal academic training. In October 1935, he returned to Berlin and was appointed chair of the renowned Department of General and Theoretical Electrical Engineering and acting Professor of Telecommunications at the Charlottenburg Institute of Technology. Soon thereafter, however, he changed careers to take on management positions at Siemens & Halske. The repeated switching between academic and industrial facilities was typical for Küpfmüller's career path.

Beginning in 1940, he conducted research salient for the wartime effort in a supervisory capacity on communication engineering first as representative of the German High Command of the Wehrmacht and later as Director of the Commission on Communication Engineering in the German Army Ordnance Office [Heereswaffenamt] and Director of the Scientific Command Staff of the German Navy<sup>62</sup> (Küpfmüller continued to be regarded as a leading authority on communication engineering<sup>63</sup>), and was highly decorated at the end of the war.

<sup>&</sup>lt;sup>57</sup> See Tab. 1 in Druckrey and Küpfmüller (1948): p. 256.

<sup>&</sup>lt;sup>58</sup> Published preliminarily in Druckrey (1943).

<sup>&</sup>lt;sup>59</sup> Cf. note 57.

<sup>&</sup>lt;sup>60</sup> H. Druckrey's DFG files (cf. note 52)

<sup>&</sup>lt;sup>61</sup> For a tabular overview of life and works see Appendix 2.

<sup>&</sup>lt;sup>62</sup> "Overall director of naval research". Scalia (2000), p. 145.

<sup>&</sup>lt;sup>63</sup> Küpfmüller was "widely considered the best authority on communications technique", Scalia (2000), p. 223.

Little is known about the content of his research during this time. <sup>64</sup> In the literature, there is the following comment:

Küpfmüller, who had conducted research on the use of different geometric shapes to hinder underwater detection, concluded that the most effective counter to Allied submarine detection consisted of a combination of 3 methods: Use of Schnorchel to avoid radar contact, use of geometrical angles and shapes to deflect radiation, and application of absorbent materials.<sup>65</sup>

In 1937, Küpfmüller became a member of the SS after having served on the staff of an SA brigade during his time in Danzig.<sup>66</sup> As the war progressed, he was promoted in the SS multiple times, at the end to Lieutenant Colonel of the SS [Obersturmbannführer]<sup>67</sup> After the end of the war, he lost his position with Siemens & Halske and was interned in various camps of the Allied Forces including Dachau and later in Hammelburg/Unterfranken.<sup>68</sup> He was freed in December 1947.<sup>69</sup>

#### Productive Internment

Besides Druckrey's vague allusions mentioned previously, there are only very few references in the published literature about Druckrey's and Küpfmüller's internment after the war. In his obituary on Druckrey, Bannasch described a "period of imprisonment" after 1945.<sup>70</sup> In his laudatory speech on Küpfmüller's 60<sup>th</sup> birthday, Druckrey also mentioned a "long confinement" after the "collapse."<sup>71</sup> Later, an obituary on Küpfmüller reads as follows:

The Siemens house parted ways with him – as detainee. He found himself in an internment camp [...] He was also able to gain something positive from his internment: While in the camp, he met Hermann Druckrey, a young colleague in the field of pharmacology from Freiburg.<sup>72</sup> Together, they conducted a study, 'Dose-Effect Relations' that then appeared in book stores in 1949.<sup>73</sup>

Because the author of the obituary knew Küpfmüller well, this testimony can be taken as being largely authentic. It points to the fact that Druckrey and Küpfmüller actually

<sup>&</sup>lt;sup>64</sup> Cornwell (2004) and Speer (1981) do not mention Küpfmüller. In contrast, a close colleague of Küpfmüller, the radar and infrared specialist, Dr. Heinz Schlicke (born 1912) was on board the legendary submarine U-234 that surrendered to the US-Navy on May 14, 1945, on its way to Japan upon the order of the Admiral of the Fleet Doenitz based on secret documents (Scalia [2000], passim).

<sup>&</sup>lt;sup>65</sup> Scalia (2000), p. 151.

<sup>&</sup>lt;sup>66</sup> BArch (formally BDC) RS D391, 1013.

<sup>&</sup>lt;sup>67</sup> BArch (formally BDC) SSO 227-A, Küpfmüller.

<sup>&</sup>lt;sup>68</sup> Information from Dr. C. Bachmann, Bavarian Main State Archive in Munich (cf. note 51).

<sup>&</sup>lt;sup>69</sup> The denazification files from Küpfmüller could not be proven until now.

<sup>&</sup>lt;sup>70</sup> Bannasch (1995).

<sup>&</sup>lt;sup>71</sup> Druckrey (1957).

<sup>&</sup>lt;sup>72</sup> Druckrey was released from detention to Dusseldorf and relocated only later to Freiburg.

<sup>&</sup>lt;sup>73</sup> Oppelt (1980).

prepared their joint publication while interned and provides more precision to Druckrey's allusions.

Druckrey's denazification files provide information on the internment period.<sup>74</sup> Therein in May 1947, Brock complained that Druckrey was in an SS-camp even though he was not a member of the SS. Druckrey maintained in March 1948 that he had been interned for two and a half years because of "shameless denunciation" but was silent about the fact that he had been head of a SS-police institution. Druckrey continued to turn to a number of figures in science through his attorney Dr. Richard Linsmayer (Munich). Adolf Butenandt interceded for him by stating:

It would be of great value and interest to science if Druckrey could be released as soon as possible from his internment and were to be provided the possibility for the unlimited continuation of his experimental research.<sup>75</sup>

The pathologist, Herwig Hamperl (1899-1976) wrote:

I first learned that Prof. Druckrey was in an internment camp and continuing his research there from your letter dated May 2, 1947 [...]. Naturally, I view it as a tremendous loss when a mind such as Druckrey's is forced to lay fallow and his talents cannot be used for the advancement of research.<sup>76</sup>

Because the name Küpfmüller was not listed in Druckrey's DFG files or in the related report from Vienna in October 1944, it can be assumed that the collaboration between the two first began in the internment camp. It remains open whether Druckrey and Küpfmüller knew each other on a personal level before or whether they first got to know each other as detainees. Both were lucky: Although the external conditions of the camp were difficult, they were apparently good enough to enable the detainees to do some sort of scientific research. In the usual American and French prisoner-of-war camps<sup>77</sup>, in the internment camps of the Soviet occupying power<sup>78</sup> or even in the concentration camps of the NS time, this type of activity by prisoners is hard to imagine or would have been impossible.<sup>79</sup>

<sup>&</sup>lt;sup>74</sup> Druckrey's denazification files (cf. note 24).

<sup>&</sup>lt;sup>75</sup> Prof. Butenandt to Dr. Linsmayer in July 3, 1947, ibid.

<sup>&</sup>lt;sup>76</sup> Prof. Hamperl to Dr. Linsmayer on May 8, 1947, ibid. Hamperl was a member of the NSDAP and SA (Klee [2003]), Brock (Druckrey's denazification files[cf. note 24]) and Butenandt (Proctor [2000b]) had been members of the NSDAP.

<sup>&</sup>lt;sup>77</sup> See Bacque (2002) for a description of the conditions in the American and French prisoner-ofwar camps.

<sup>&</sup>lt;sup>78</sup> See Flocken and Klonovsky (1991) on Soviet internment camps.

<sup>&</sup>lt;sup>79</sup> A well-known exception pertains to the behavioral scientist Konrad Lorenz (1903-1989) who began writing his book, "Behind the Mirror" under extremely harsh conditions while in a Soviet internment camp (Fischer [2004], p. 302).

As also described by Bacque<sup>80</sup>, the registration of prisoners in American camps was not very precise. Based on the documents received, Druckrey first went to the Zell am See Camp after his arrest on May 16, 1945 and then to different detention stations (including Stefanskirchen<sup>81</sup>) and to the Hammelburg/Unterfranken camp on December 18, 1946 where he stayed until September 14, 1947.<sup>82</sup> From there he was moved to the British zone to Staumuhle Camp<sup>83</sup> and in December 1947 he was released as "exonerated" (category 5) to Dusseldorf. Apparently, Küpfmüller was also located in Camp Hammelburg from which he was released on December 16, 1947.<sup>84</sup> There is, therefore, a high likelihood that Druckrey and Küpfmüller both met and worked together in Hammelburg.

Based on this, the assumption is justified that the summation effect<sup>85</sup> and the principle of the irreversibility of carcinogenic effects were discovered in Camp Hammelburg in 1947. Only after both Druckrey *and* Küpfmüller had theoretically defined the notion of summation toxins was it possible to interpret the results of Druckrey's large-scale butter yellow experiments to the fullest extent and to recognize their importance. It was shown

[...] that the theoretical analysis of experimentally determined dose-response relations as well as of time-response relations leads to important principles that could not emerge through experimental work alone because the complexity of even the simplest biological systems causes ever changing patterns.<sup>86</sup>

On June 5, 1947, as Druckrey and Küpfmüller submitted their manuscript to the *Zeitschrift für Naturforschung* [Journal of Natural Science], both were still interned. That is the reason they could not provide an affiliation. It also may have appeared to them to be inappropriate to mention the DFG as a funding institution because of its problematic role and that of its president Mentzel during the NS time. It is amazing, however, that prisoners were permitted to submit a long manuscript with figures, whereby this was possibly handled through Druckrey's attorney. There appears also to have been contact with the publisher of *Dose-Response Effects*, Dr. Werner Saenger,<sup>87</sup> during their internment though the final manuscript was presumably completed after the release of both authors.

<sup>&</sup>lt;sup>80</sup> Bacque (2002), p. 77 ff.

<sup>&</sup>lt;sup>81</sup> Druckrey named this camp in a questionnaire during his denazification, Druckrey's denazification files (cf. note 24).

<sup>&</sup>lt;sup>82</sup> Information from Dr. C. Bachmann, Bavarian Main State Archive in Munich (cf. note 51).

<sup>&</sup>lt;sup>83</sup> Druckrey's denazification files (cf. note 24).

<sup>&</sup>lt;sup>84</sup> Cf. note 51.

<sup>&</sup>lt;sup>85</sup> Summation toxins: "For these toxins, it is not simply the level of concentration of the toxin, C, alone that is decisive as is primarily the case for the other "concentration toxins", but rather also the duration over which the effect stretches." Druckrey and Küpfmüller (1948), p. 607. Cf. Dekant and Vamvakas for a recent presentation.

<sup>&</sup>lt;sup>86</sup> In Druckrey and Küpfmüller (1949), p. 644.

<sup>&</sup>lt;sup>87</sup> The authors thanks Saenger "for his meritorious support of the book under difficult circumstances (Druckrey and Küpfmüller, 1949, p. 514). In other places, Druckrey described the term "circumstances" as being the internment camp, e.g., Druckrey (1957).

### The Interdisciplinary Solution

The possible dependence of the carcinogenic effects on dosage had been of interest to Druckrey for years. In a programmatic article<sup>88</sup> in July 1942, he interpreted chemical agents causing cancer to be pharmacological effects and also discussed the dose-response he expected and confirmed through his own, initial experiments. A short time later, Druckrey<sup>89</sup> published the preliminary results of his large-scale butter yellow experiments under the title, *Quantitative Foundations of Carcinogenesis*.<sup>90</sup> Already in this study, carcinogens are categorized in terms of the so-called "c x t-toxin" (Concentration x time). The time factor was unusually high and therefore not readily interpretable. Whereby only limited times in the magnitude of a few days, at most, were known for c x t-toxins, here time stretched out into years. It was at this stage of the research that the interdisciplinary research began. A comparison of the work completed in 1943 and 1948 makes the progress very clear that was achieved through the collaboration with Küpfmüller. In 1943, the term "quantitative" referred primarily to conducting the experiments, i.e., determining the time between the emergence of the first tumors (latency time) after application of different dosages per day and graphically representing the interdependencies. Because the dose-response curve followed a hyperbolic curve, the natural conclusion was that it has to do with a c x t-toxin. The "clear mathematical relationship"<sup>91</sup> between dose and latency time was obtained through simple multiplication: Dose x Time = Constant. In contrast, on the basis of, naturally, the same experimental procedures, the Quantitative Analysis of Carcinogenesis from 1948<sup>92</sup> contains a primarily mathematically based analysis of the experiments, including a precise delineation of the mechanism of action assuming simple reaction kinetics and the estimation of the probability of cancer cells emerging within a restricted period of time. With the collaboration of Küpfmüller, there was a notable shift from an empirical to a precision-based scientific perspective, from the experiment to the theory, from a careful compilation of test data to a strict, mathematical proof. Only the latter allowed for the formulation of the theory that postulated that the carcinogenic effect of chemical compounds is a function of the total dosage (sum of all individual doses throughout one's lifetime; "summation effect"). In addition:

> Over the course of years of experiments, cell divisions frequently took place such that individual doses were no longer affecting the original cells, but rather the daughter cells. If by every cell division there was also a division of the effect, then the total dosage required for cancer induction would also have had to increase with the same frequency with which the cells were dividing, that is, the longer the latency period in the experiment. Our experiments, however, required the smallest total dosage for the longest test durations. The primary effects, therefore, persist in the daughter cells and are capable of summation.

<sup>&</sup>lt;sup>88</sup> Druckrey (1942). This essay was dedicated to Heubner for his 65<sup>th</sup> birthday.

<sup>&</sup>lt;sup>89</sup> The author characterized himself as "the resident physician in the East."

<sup>&</sup>lt;sup>90</sup> Druckrey (1943)

<sup>&</sup>lt;sup>91</sup> Druckrey (1943), p. 534.

<sup>&</sup>lt;sup>92</sup> Druckrey and Küpfmüller (1948).

They did not "thin out" through cell division, but rather contributed to the reduplication. The specific cell receptors that the carcinogenic agencies attack have to *be substances that are capable of self-reproduction*. [...] The strength of their [the cancer-producing substances'] effect must, *on the one hand, be strong enough to produce genetic changes to an extent large enough for autonomous behavior, but, on the other hand, not be too large so as to produce lethal effects*.

Druckey later described with precision Küpfmüller's contribution to the publication of the monograph, *Dose-Effect Relations*: It was

[...] the analysis of the carcinogenic effect that led to collaborating with Karl Küpfmüller on pharmacological matters. Out of this emerged the necessity to test for the principles underlying the effects of toxins and drug efficacy. The results of these analyses that were completed under seemingly disadvantageous conditions are summarized in the book, "Dose-Effect Relations" [...] as an attempt at a theoretical pharmacology. These results led Küpfmüller in 1947 to construct an electrical model that must be described as one of the first calculators that could calculate the complex processes of resorption and the distribution of toxins in the body, its detoxification, and excretion in a fraction of a second through the use of equations and differential equations.<sup>94</sup> The experiments on the kinetics of pharmacological effects conducted in the second half of the book make the connection to chemical reaction kinetics, the law of mass effects, the hyperbolic curve of the dose-response relationship from A. J. Clark<sup>95</sup>, and the "hit theory"<sup>96</sup> in biophysics. In addition, in classifying the physical dimensions, they provided clear definitions of the most important pharmacological terms and the factors influencing them. An area of special interest to Küpfmüller is how "control systems" regulate life processes and their meaning for physiology and pharmacology. Herein lies the particularly close relationship to electrical engineering.<sup>97</sup>

Küpfmüller was able to incorporate his diverse interests in the development of the field of theoretical pharmacology. Approximately half of the text is in the form of formulas which is not common in medical papers. For Küpfmüller, the realization of his ideas in the area of pharmacology may have been a type of proof of principle of his systems theory as applied to biological problems.<sup>98</sup>

<sup>&</sup>lt;sup>93</sup> Druckrey and Küpfmüller (1948), p. 263 f. Emphasis in original.

<sup>&</sup>lt;sup>94</sup> One device constructed based on plans by Küpfmüller was successfully tested by Rhode & Schwarz in Munich, Druckrey and Küpfmüller (1949), p. 590.

<sup>&</sup>lt;sup>95</sup> Druckrey is referring to an article published in 1937 by Alfred J. Clark (1885-1941) in Heffter-Heubner's Handbook of Experimental Pharmacology, Supplement 4, Berlin (ibid, p. 515).

<sup>&</sup>lt;sup>96</sup> In quantum biology, processes that appear as a result of penetrating rays are triggered through individual microphysical events (hits).

<sup>&</sup>lt;sup>97</sup> Druckrey (1957).

<sup>&</sup>lt;sup>98</sup> In his book, "The Systems Theory of Electrical Information Transmission" that was based on lectures held between 1937 and 1943 (Schoen [1994]) and published in 1949, Küpfmüller characterized the term, systems theory (today: theory of dynamic systems) as a new discipline in science that developed especially under the influence of the theory of information transmission but also biology. One paper by Küpfmüller's from 1924 is viewed as the genesis of systems theory

In systems theory, systems of transmission are characterized by a few dimensions which are freely disposable without initially taking their execution into account. In this way, all fundamental questions can be separated from the complications caused by coincidence circuits or arrangements. This simplifies the experiments and allows the most relevant aspects of the processes to be recognized. The real systems can be observed or produced as an approximation of the assumed characteristics.<sup>99</sup>

Both researchers could have their visions realized through the results of these works: Druckrey in his hypothesis that cancer caused by chemical substances is a special type of pharmacological effect that can be quantitatively measured and described as such,<sup>100</sup> and Küpfmüller in his perspective that biological phenomena or principles are also accessible through precise mathematical treatment that can allow the nature of these processes or the causal mechanisms that underlie them to be recognized.<sup>101</sup> Prior to this, Druckrey had never relied on such a rigorous line of evidence to interpret his tests.

Barriers between the different disciplines that, as experience has shown, stand in the way of cooperation did not play an important role in this concrete instance because Druckrey and Küpfmüller could quickly understand one another due to their kindred visions. The external circumstances of internment may have actually simplified their collaboration because there was ample time for discussion and both researchers needed to prepare themselves for a new direction in their civilian careers at the end of the war. As experienced university professors, they were very familiar with the principles of their fields even without access to the literature.

(Wunsch [1997]). Ludwig von Bertalanffy (1901-1972) developed similar concepts at approximately the same time in the field of biology in "General Systems Theory" (1950). <sup>99</sup> Küpfmüller (1949), p. 6.

<sup>&</sup>lt;sup>100</sup> Druckrey (1942).

<sup>&</sup>lt;sup>101</sup> cf. note 98.

#### Druckrey's Academic Fate after 1945

While Küpfmüller found a position in academia at the beginning of the 1950s that was appropriate given his scientific accomplishments, Druckrey was denied a similar recognition. Primarily with the support of DFG and after a few rocky initial years, he was able to conduct scientific research under very good conditions. He was also able to rally staff around him (including Dietrich Schmaehl, Stefan Ivankovic, and Rudolf Preussmann) and doctoral students (including Peter Bannasch, Manfred F. Rajewsky, and Gerhard Eisenbrand) of which many later became respected researchers. Nevertheless, he was not able to continue his earlier profession as a university professor which was, in his view, his true role. The positions he obtained were not commensurate with his actual rank in his field. A few honors awarded to him later, primarily from other countries, could not change that.

As Adjunct Professor, Druckrey was, from 1948 to 1964, the Director of a laboratory at the Department of Surgery at Freiburg University Hospital (Breisgau) under the directorship (until 1952) of Eduard Rehn (1880-1972) and (beginning in 1952) of Hermann Krauss (1899-1971). In 1952, the laboratory achieved the status of "the DFG Research Unit of Preventive Medicine." In 1964, they moved into their own building at the Max Planck Institute of Immunobiology in Freiburg. The Research group existed until 1973 when Druckrey retired.<sup>102</sup>

It is assumed that Druckrey's "participation in National Socialism during the Third Reich had a negative influence on his further academic career after 1945."<sup>103</sup> This is true with conditions. There are numerous examples<sup>104</sup> of careers continuing unimpeded after 1945 despite a strong involvement in the Third Reich. Why didn't this happen to Druckrey?

A court of the Dusseldorf municipality categorized him as a category 4 (follower) without a freezing of assets on April 8, 1948.<sup>105</sup> No employment restrictions were associated with this categorization. The court judged the numerous incriminating statements as being "highly subjective." It was beneficial to Druckrey that many opinions referred to his undeniable scientific qualifications. After this decision, the entire academic world should have been open to him again.

- <sup>103</sup> Quote from Nachruf Bannasch (1995); see also Eckart (2000), p. XVIII.
- <sup>104</sup> Klee (2003).

<sup>&</sup>lt;sup>102</sup> Boyland (1974).

<sup>&</sup>lt;sup>105</sup> Druckrey's denazification files (cf. note 24).

Druckrey's personal behavior at the University of Berlin, especially the dispute with his academic advisor Heubner in the winter of 1942/43 was fresh in many people's minds and stood in the way of his reintegration. The opinion of Heubner, who was highly regarded and who had consistently rejected National Socialism, was heavily weighted in the circle of academic colleagues.

I myself would personally welcome it if Druckrey could find the opportunity to continue to conduct scientific research in some form, but would also regard it as regrettable if he were to obtain a leading position in a university and then obstruct colleagues with more sympathetic political or human qualities.<sup>106</sup>

Lendle made a similar statement:

I would regret it if D. would be completely shut off from conducting scientific research. On the other hand, an appointment in a department in our field or in a leadership position at, say, the Kaiser-Wilhelm Institute for Biological Research, cannot be recommended.

He explained further:

He was widely unpopular within the circle of colleagues due to his excessively inflated self-esteem and arrogant criticism of older colleagues. When my successor was summoned in Munster, his discussion with the department there was not possible because the department representatives that knew him (mostly members of the Party) rejected him as impossible.<sup>107</sup>

And just as Heubner and Lendle recommended, that is what Druckrey experienced: no appointment to a university position and all opportunities to conduct scientific research.

If Druckrey was not successful in continuing his academic career path after 1945, it presumably was largely due to his earlier, less-than-academic behavior and not because he was a devoted and active National Socialist. The former was unforgiveable in the academic world while the latter was viewed as a permissible sin, as evidenced by so many careers after 1945.

## Discussion

In the history of cancer research, the names Druckrey and Küpfmüller together stand for the introduction of a mathematical model of the dose-effect relationship in chemical cancerogenesis. The summation effect and the therein implied irreversibility of

<sup>&</sup>lt;sup>106</sup> Heubner to F. Jung on January 30, 1948, per Scheler and Oehme (2002), p. 71.

<sup>&</sup>lt;sup>107</sup> Prof. Lendle to the denazification committee on February 11, 1948, Druckrey's denazification files (cf note 24)

carcinogenic effects was described long before the respective target molecules were identified. Today we know the cause because we know that even the smallest doses of carcinogenic substances can verifiably bring about genetic modifications. The uncontrolled growth of a cell can be triggered through persistent and accumulating genetic modifications. The discovery of the summation effect is to be seen as one of the most important roots of the modern study of cancer. Although it happened rather coincidentally, it is an early example for the success of interdisciplinary collaboration in the field of cancer research. Because representatives of the participating disciplines had not collaborated before, the outcome is particularly innovative.

The external circumstances of the collaboration were complicated, but at the end also extraordinarily lucky. It should not be forgotten that both researchers were interned due to their active involvement in the NS-system. In addition to his high SA-rank, Druckrey had most recently been the director of an SS-Police Institute and it was also assumed by CIC that his Vienna Institute took part in SS medical crimes. As chief military officer for the SS and top researcher in defense research,<sup>108</sup> Küpfmüller had to accept a high level of personal responsibility for German warfare experiences. So the long internment was not a completely unearned fate. Only when a direct perpetration could be ruled out or could not be proven were both freed and they quickly found new areas of activity in their original professions. Both, but especially Druckrey, were able to build on the foundations laid while in captivity.

Besides the coincidence that was decisive for Druckrey and Küpfmüller meeting each other, there are other factors conducive to innovation that should not be ignored. This includes the visions of both researchers that were surprisingly complementary, the interdisciplinary coupling of their areas of science, and a creative environment that both had experienced already during their training. Such factors count as key elements for new ideas in research and development.<sup>109</sup> Fate can be interpreted in this context as the intercept point between two causal lines (cancer research or pharmacology and mathematics or systems theory).<sup>110</sup>

Druckrey's and Küpfmüller's results count among those of the "partly creative and even groundbreaking research programs of the NS era. In no way should we forget the criminal NS-experiments in the concentration camps [...], but we should also not forget that a

<sup>&</sup>lt;sup>108</sup> Federspiel (2002), p. 98. Küpfmüller was, among other things, head of the research staff of the German Navy.

<sup>&</sup>lt;sup>109</sup> Duechtung (1994).

<sup>&</sup>lt;sup>110</sup> Ibid. A coincidence is the "unplanned meeting of two occurrences" (The New Brockhaus, 7<sup>th</sup> edition, Wiesbaden 1985) or "something that was not foreseen or was not intended or occurred unexpectantly" (Brockhaus Encyclopedia, 19<sup>th</sup> Edition, Mannheim 1995). It was a coincidence that Druckrey and Küpfmüller met in the same camp at the time and were there long enough to implement their innovation. Moreover, it is not a trivial matter that Druckrey met a researcher while in the internment camp that helped him to correctly interpret his own test results that previously had been inexplicable.

number of non-negligible innovations in the area of *cancer etiology* [emphasis by VW] were launched and developed under the NS dictatorship," ascertained the American historian, Robert Proctor.<sup>111</sup>

From the perspective of today, the question whether loyal National Socialists can also make good researchers can be answered in the affirmative. According to Proctor,<sup>112</sup> Butenandt's [very subjective] standard argument after 1945 was: Whoever conducts real research cannot have been a Nazi; scientific productivity was evidence of political innocence. Now Druckrey and Küpfmüller were very good and productive scientists. According to the verdict of contemporary witnesses,<sup>113</sup> at a minimum, Druckrey was simultaneously a Nazi activist<sup>114</sup> (The author did not have the corresponding reports on Küpfmüller; he was also not "politically innocent"). Even Butenandt could not refrain from attributing both attributes to Druckrey, who he knew a long time. Nevertheless, in 1947, he had still characterized him with regards to National Socialism (what appears strange today) as an "idealist of noble disposition and bearing."<sup>115</sup>

Wolfgang Heubner also faced criticism in connection with the post-1945 culture of "Persilclean certificates" [*TN*: The "Persilschein was a certificate of good standing named after the laundry detergent, Persil, in which former association with the NS could be "washed clean" based on character testaments. ], that was also cultivated by Butenandt <sup>116</sup> His differing testimony in Druckrey's denazification files provided, however, anything but a Persil-clean certificate ["Persilschein"]. It presented a balanced judgment of the incriminating and exculpating elements in the Vita of the accused and provided clear recommendations that were also later followed. Considering Druckrey's later accomplishments in the area of cancer research, it would have been in no way responsible to deny him an active research program. Heubner's motivation in the case of Druckrey was however completely different than that evidenced in his collaboration in the controversial Verschuer memorandum of 1949.<sup>117</sup>

Whereby Druckrey "never concealed his conviction regarding the excellence of National Socialist ideas"<sup>118</sup> until 1945, Küpfmüller was more a political conformist. Nevertheless, we only have a few biographical details on both researchers, particularly for the years

<sup>&</sup>lt;sup>111</sup> Proctor (2000 a), p. 74.

<sup>&</sup>lt;sup>112</sup> Proctor (2000 b), p. 34, quoted in Klee (2001), p. 353.

<sup>&</sup>lt;sup>113</sup> Statements by Dr. F. Bergmann, Prof. R. Havemann, Lisa Heubner, Prof. W. Heubner, Dr. F. Jung, Ingeborg Klempau, Prof. L. Lendle, Dr. W. Loch, Margarete Stuhlmann. Besides Butenandt, Prof. B. Behrens, Dr. N. Brock, Dr. P. Marquardt, Prof. G. Orzechowski and Dr. W. Trappe also held him for a NS-idealist (see cf. note 24).

<sup>&</sup>lt;sup>114</sup> Without citing a source, Proctor (1999) called Druckrey a "Himmler confidante." (p. 130). Elsewhere it is stated: "Druckrey was an eager National Socialist ... (and a very good scientist, I should add)." p. 255

<sup>&</sup>lt;sup>115</sup> Prof. Butenandt to Dr. Linsmayer on July 3, 1947, Druckrey's denazification files (cf. note 24). For more on Butenandt's position during the NS era, see Proctor (2000 b).

<sup>&</sup>lt;sup>116</sup> Sachse (2002), passim.

<sup>&</sup>lt;sup>117</sup> See also ibid.

<sup>&</sup>lt;sup>118</sup> Heubner 1948, Druckrey's denazification files (cf. note 24).

between 1943 and 1945. Additional research appears, therefore, to be appropriate. The guiding principle for such efforts should be: "The most honest form of apology is [...] the disclosure of guilt. For researchers, this should be, perhaps, the most appropriate form of apology."<sup>119</sup>

## Appendices

## Appendix I: Hermann Druckrey's Curriculum Vitae

Druckrey, Hermann Karl Paul, born July 27, 1904 in Greifswald (father: pharmacist), died August 7, 1994 in Freiburg im Breisgau. Professor, medical doctor, pharmacologist, cancer researcher. Facts until 1944 are self-reported, see BArch (formerly BDC) SA 109, DS B28, partially previously published by Hubenstorf (1989), Deichmann (2001) and Klee (2003).

## Academic Career

1923 1923-1926	Secondary school leaving examination ["Abitur"] in Quedlinburg, Germany Pharmacist training
1926-1931	Medical school in Giessen and Heidelberg, State examinations in Leipzig, Germany
1930-1931	Visiting scholar at the Institute for Experimental Pathology, University of Prague (Prof. Biedl), Czechoslovakia
1932	Doctorate at the University of Leipzig, gynecological clinic (Privy Councilor Sellheim)
1933	Visiting scholar for 6 months at the Chemistry Department of the University of Gottingen (Prof. Butenandt).
1933	Assistant, Pharmacological Institute, University of Berlin (Prof. Heubner)
1936	Postdoctoral qualification ["Habilitation"] at the Pharmacological Institute, University of Berlin
1936	First research contract on the topic of cancer
1939	Senior assistant, Pharmacological Institute, University of Berlin
1942	Professor of Pharmacology and Toxicology, University of Berlin
1943	Departure from the university upon his own request (?)
1948	Laboratory Head, Department of Surgery at Freiburg im Breisgau University Hospital.
1952	Director of the DFG Research Unit of Preventive Medicine, University of Freiburg im Breisgau.
1953-1974	Chair of the Dyestuff Commission of the DFG
1964	Director of the research group on preventive medicine at the Max Planck Institute of Immunobiology in Freiburg im Breisgau.
1973	In retirement

<sup>&</sup>lt;sup>119</sup> Markl (2003), p. 51.

## Noteworthy Scientific Accomplishments

Breeding of genetically homogenous rat strains, proof for summation effects and enhancement effects and of organotropic effects of chemical carcinogenesis, animal models for tumors of the central nervous system, prenatal production of cancer, transport and active form of chemotherapeutics.

## Honors

1955	Scheele Medal
1973	Salzer Prize for cancer research
1973	Cover story, Cancer Research
1973	Honorary member of the Japanese Cancer Association
1979	Honorary member of the American Association of Cancer Research
1981	Citation Classic
1984	Honorary doctorate from the Department of Medicine of the University of
	Hamburg

Acknowledgements in Brock (1964), Hamperl (1974), Boyland (1979), Kleihues & Magee (1994). In the obituary, Bannasch (1995) briefly mentioned the NS time.

## National Socialist Career

Member of the Viking-League/Ehrhardt-Brigade
Member of the NSDAP, No. 475.138 in Leipzig
Entry into SA and rapid ascent: 1935 Lieutenant Colonel of the SA, 1940 SA-Colonel. 1943 Senior Colonel
Representative of the NS-Lecturer Association at the Department of Medicine, Berlin
Military physician of the SS-Police regiment of East Front/Russia <sup>120</sup>
Director of a Pharmacological Institute of the police in Vienna created just for him (Vienna VII, 62, 19 Apollogasse) that were headed by the Reich physician-SS and the police. Druckrey referred to a priority command by the Reich physician-SS and the police on June 3, 1944. Military advisor regarding toxicology.
Chief Staff Surgeon Chief of the Reserve Police
Arrest by the American CIC
Internment in Allied Forces camps
Denazification in Dusseldorf municipality.

<sup>&</sup>lt;sup>120</sup> For his service in Russia as battalion physician in Gottberg's combat group (Regiment 24), Druckrey received the iron cross second class on December 17, 1943 (Federal Archives/Central Verification Office Aachen Signature RH 7 A 1334.23, Information dated January 14, 2005). For information on the commander of the combat group, SS –Senior Group Leader, Curt von Gottberg (1896-1945), see Klein (2004); for information on the different deployment sites, in 1943-44, primarily to combat partisans in Belarus, see Schulz and Wegmann (2003).

## Appendix II: Karl Küpfmüller's Curriculum Vitae

**Küpfmüller**, Christian Friedrich **Karl**, Born October 6, 1897 in Nurnberg (Father was a locomotive driver) died December 26, 1977 in Darmstadt, Germany. Professor, honorary doctor of engineering, electrical and communication engineer.

Information from Schoen (1994) and <u>http://www.fh-sw/fachb/et/ahnentafel/daten/zukupf.html</u>, supplemented by self-portrayals, see BArch (formerly BDC) RS D391, 1013.

## **Professional Career**

1914-1915	Practical training in electrical engineering at the Siemens-Schuckert plants in Nurnberg
1915-1916	Attended the Nurnberg Higher Technical Institute
1916-1918	Infantry man in the First World War
1919	Degree in electrical engineering after four semesters in Nurnberg
1919-1921	Assistant to K. W. Wagner at the Telegraph Technical Office of the Reich in Berlin
1919	Secondary school leaving examination ["Abitur"] in Berlin
1921-1928	Senior engineer at the main laboratory at Siemens & Halske in Berlin (including research on malfunctioning in remote cables and measures to correct them. 1924: relationship between settling time and bandwidth in linear systems (Küpfmüller's uncertainty principle). First discourses on system theory
1928-1935	Full Professor of electrical engineering at the Institute of Technology in Danzig
1935-1937	Full Professor of electrical engineering at the Institute of Technology in Berlin, joint appointment in the Department of Telecommunications
1937-1945	Appointment at Siemens & Halske again, this time as Director of the Development of Communication Engineering at the Werner Plant for Telecommunications and beginning in 1941, Director of Technical Development (Director and Chief Representative). Honorary professor at the Institute of Technology in Berlin.
1946-1948	Research Development at Rohde & Schwarz in Munich, partially interrupted through internment
1948-1952	Director of Research Development and board member of the "Standard Electricity Society (Later, the SEL) in Stuttgart
1951-1952	Honorary Professor at the Stuttgart Institute of Technology
1952-1963	Full Professor and Director of the Institute for Communication and
	Technology at the Darmstadt Institute of Technology (TH)
1955-1956	Chancellor of the Darmstadt TH
1955-1957	Vice President of the German Research Foundation
1963	Fmeritus.

## Special Scientific Accomplishments

Küpfmüller was broadly active in electrical engineering, in particular in the areas of communication, measurement and control engineering, acoustics, information theory, and theoretical electrical engineering; successful both in industry and academic teaching. His contributions to communication transmission engineering and his systems theory are outstanding. Standard reference text: *Introduction to Theoretical Electrical Engineering* (1<sup>st</sup> edition 1932; 16<sup>th</sup> edition 2005), *The Systems Theory of Electrical Communication Technology* (1<sup>st</sup> Edition 1949; 4<sup>th</sup> Edition 1974) (http://www.nue.tu-berlin.de/history/kuepfmueller.htm)

## Honors

1932	Gauss-Weber Commemorative Coin of the University of Gottingen
1944	Honorary doctorate of the Danzig TH
1953	Philipp Reis Plaque of the German Federal Postal Administration
1954	Corresponding member of the Bavarian Academy of Sciences
1954	Member of the Academy of Sciences and Literature in Mainz
1959	Golden Cedergren Medal of the Swedish Institute of Technology
1960	Golden Stefan Medal of the Austrian Association of Electrical Engineering
1962	Honorary Ring of the German Association of Electrical Engineers
1968	Werner-von-Siemens Ring
1969	Honorary President of the German Society for Cybernetics
1976	Honorary doctorate of the University of Erlangen-Nurnberg
1977	Foundation for the "Karl-Küpfmüller Ring" by the Darmstadt TH (10
	recipients so far, with Prof. Ernst Dieter Gilles, 2005 being the latest)
1979	Foundation for the "Karl-Küpfmüller Award" of the Communication
	Engineering Society NTG (today: ITG) (awarded every four years, with the
	latest award to Prof. Kurt Antreich, 2004)

Acknowledgements in Gundlach (1962), Anonymous (1977), Interview with the Communication Engineering Newspaper NTZ (1977), Oppelt (1980), Mielert (1982), Mauel (1983), Bissell (1986), Kind and Muehe (1989) and Wunsch (1997). Druckrey's contribution is particularly informative in the context of this paper (1957).

## National Socialist Career

Member of the NSDAP (beginning May 1, 1937, No. 4. 834.225), of the SA (from August 1, 1933 until April 1, 1937) and the SS (beginning July 1, 1937, No. 294.587) (all information is first hand from Küpfmüller). Promotion within the SS: 1940 SS-1st Lieutenant, 1942 Captain, 1943 Major, beginning April 20, 1944: Lieutenant Colonel. Marriage in 1941 likely obtained the personal permission of Reichsführer-SS Himmler (BArch [formerly BDC] RS D391, 1013 and SSO 227-A, Küpfmüller).

1940	Leadership position charged by the High Command of the German Armed Forces with the responsibility of the development and production of all telecommunication equipment (BArch [formerly BDC]] SSO 227-A)
1942	Director of the Commission of Communication Engineering in Military
	Weapon Systems
	(http://www.aleph99.org/etusci/ks/t2a10.htm)
1943	War Merit Cross First Class With Swords, (BArch [formerly BDC] SSO
	227-A)
1944 or 1945	Knight's Cross of Military Valor with Swords as Director of the Research Leadership Staff of the Navy <sup>121</sup>
	(http://www.deutsche-marinesoldaten.de/lebenslaeufe/liste-ritterkreuz-
	<u>kvk.htm</u> )
1944	Dr. Fritz Todt Prize in Gold (funded in February 1944 for the first time) for
	the development of decisive improvements in the area of weapon
	production (BArch [formerly BDC] SSO 227-A)
1946-1947	Internment in Allied Forces camps

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<sup>&</sup>lt;sup>121</sup> Attempts to locate information on Küpfmüller's activities in the Navy in the collection of the Federal Archives-Aachen Central Verification Office were not successful (correspondence from April 7, 2005).

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Archival Sources

BAK	Koblenz Federal Archive, R73, German Research Foundation
BArch	Berlin-Lichterfelde Federal Archive. R26, Reich Research Council
BDC	Berlin Document Center (now Berlin-Lichterfelde Federal Archive) DS
	Diverses, PK Party Correspondent, RS Administration of Race and
	Settlement Main Office, SA Storm Division, SSO SS-Führer personal files
HStAD NW	North Rhine-Westphalia, Dusseldorf Central Archives

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