## The whole truth and nothing but the truth? The research that Philip Morris did not want you to see



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The tobacco industry maintained, for many years, that it was unaware of research about the toxic effects of smoking. By the 1970s, however, the industry decided that it needed this information but they were unwilling to seek it in a way that was open to public scrutiny. By means of material from internal industry documents it can be revealed that one company, Philip Morris, acquired a research facility, INBIFO, in Germany and created a complex mechanism seeking to ensure that the work done in the facility could not be linked to Philip Morris. In particular it involved the appointment of a Swedish professor as a 'co-ordinator', who would synthesise reports for onward transmission to the USA. Various arrangements were made to conceal this process, not only from the wider public, but also from many within Philip Morris, although it was known to some senior executives. INBIFO appears to have published only a small amount of its research and what was published appears to differ considerably from what was not. In particular, the unpublished reports provided evidence of the greater toxicity of sidestream than mainstream smoke, a finding of particular relevance given the industry's continuing denial of the harmful effects of passive smoking. By contrast, much of its published work comprises papers that convey a message that could be considered useful to the industry, in particular casting doubt on methods used to assess the effects of passive smoking.

http://image.thelancet.com/ extras/03art7306web.pdf OxyRomandie, Geneva, Switzerland (P.A. Diethelm):

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For several decades the tobacco industry maintained that evidence of adverse health consequences of its products was at best inconclusive and that they were actually socially responsible companies concerned about the health of their customers, a view first expressed in a statement published in American newspapers in 1954 stating that "We accept an interest in people's health as a basic responsibility, paramount to every other consideration in our business". 1 More recently, however, even the tobacco industry has recognised that its position with regard to the health effects of active smoking has been untenable, as summarised by the UK House of Commons Health Committee in 2000: "It seems to us that the companies have sought to undermine the scientific consensus until such time as that position appears ridiculous."2 Yet, as the committee continued: "So the companies now generally accept that smoking is dangerous (but put forward distracting arguments to suggest that epidemiology is not an exact science, so that the figures for those killed by tobacco may be exaggerated); are equivocal about nicotine's addictiveness; and are still attempting to undermine the argument that passive smoking is dangerous." One of the most public examples of the industry's stance was in hearings before the US Congress in 1994, when chief executive officers of the seven largest American tobacco companies each testified that nicotine was not addictive,<sup>3</sup> even though internal documents showed that they knew this not to be the case. Thus, as long ago as 1963, an industry document stated that "Nicotine is addictive. We are, then, in the business of selling nicotine—an addictive drug effective in the release of stress mechanisms."4 Indeed, in the late 1960s, The American Tobacco Company even explored the feasibility of using the stalks of the plant Nicotiana rustica for commercial production of nicotine content to be added to cigarettes.<sup>5</sup> More recently, other authors have published work that suggests the existence of a major campaign waged by the industry to undermine the evidence on the health effects of passive smoking.<sup>67</sup>

One of the arguments advanced to sustain these positions was that the industry was unaware of any biological evidence on the harmful effects of smoking and, in particular, that it did not conduct such research. As one senior scientist in Philip Morris noted, in "defending corporations from the claims of heirs and estates of deceased smokers," their position was that "We within the industry are ignorant of any relationship between smoking and disease. Within our laboratories no work is being conducted on biological systems".8 In reality, however, this was not entirely true, as we show in this paper that describes the work of a facility established by Philip Morris that would enable it to conduct biological research without acknowledging involvement in it. In our view, this provides further evidence of the way in which the transnational tobacco industry sought to use scientific research to advance its own interests.

Under a 1998 legal settlement with the State of Minnesota, six leading tobacco companies were required to make public millions of pages of their internal records in depositories in Minnesota and Guildford. The subsequent Master Settlement Agreement stipulated that, with the exception of British American Tobacco and the Liggett Group, they post their documents on public websites, along with documents from the research-funding agency Council for Tobacco Research and the Tobacco Institute. Additionally, two private websites were created: Tobacco Documents Online and the Legacy Tobacco Document Library, the latter at University of California, Francisco. Specific searches were made on the Tobacco Documents Online (http://www. tobaccodocuments.org), Legacy Tobacco Document Library (http://legacy.library.ucsf.edu), and Philip Morris (http://www.pmdocs.com) sites initially using the terms INBIFO and names of individuals known to be associated with its work. This search was supplemented with material identified by searching the internet using Google (http://www.google.com), again with the initial term INBIFO. Published research from INBIFO was identified with PubMed. Subsequent searching was iterative, following up leads generated in individual documents to trace sequences of events. Finally, additional material was obtained from investigations undertaken as part of the defence and from subsequent discovery and disclosures in a legal case in which two of the authors (PAD, J-CR) were defendants and the third (MM) was a witness.

It appears that the need to develop capacity to undertake biological research was first identified by Philip Morris in 1968, when one of its vice-presidents, Helmut Wakeham, highlighted the threat arising from "the opponents of smoking [who] are effectively playing on the fears of the public". Until then, Philip Morris had depended on a "technical intelligence system" to alert them to scientific developments but this was apparently failing to meet their needs as information often came after publication and much of the then available research was from studies "oriented to seeking out and highlighting the negatives associated with tobacco smoke".9 As a consequence, there is evidence that Philip Morris foresaw a need to "obtain our own facts and data in biological systems, in order to avoid being surprised by information from outside sources and in order to interpret and understand the results of such studies".9 According to Wakeham, Philip Morris had reasons to believe that other companies were following a similar path; he pointed out how, for example, biomedical research undertaken by another tobacco company had been "relocated under conditions of extreme secrecy . . . to new research facilities".9

The following year, Philip Morris prepared a business case for a new biological research facility. Also written by Wakeham, it argued that "We believe that this program can be carried out most economically and effectively by the establishment of an in-house facility". It then identified types of research that would be conducted in such a facility, including inhalation studies, where the objective would be "The determination in different animal species of the acute and chronic effects of smoke from various tobaccos" and "Tests for carcinogenic activity", arguing that, although mouse studies "have questionable relevance to humans, these tests are accepted by most investigators as the most reliable indicator for carcinogenic activity."

The paper concluded that "We must know more about our products than anyone else so that we are not surprised when our competitors or our antagonists publish information about our products. We must know how our products perform in conventional tests regardless of whether or not we believe them to be significant".

The argument that Philip Morris should undertake such research was not, however, viewed enthusiastically by its chairman and chief executive officer, Joseph F Cullman, who had "serious reservations about the wisdom of embarking upon this program at this time". However his concerns were allayed after a meeting with Wakeham when, while stating that work already being undertaken in Boston was "as far as we should go now", Cullman agreed that research "on a contractual basis in Europe ... presents an opportunity that is relatively lacking in risk and unattractive repercussions in this country". 12

An opportunity presented itself later in 1970 when a research facility in Germany, the Institut für Industrielle und Biologische Forschung GmbH (INBIFO) came on the market. Wakeham advocated the purchase of INBIFO by Philip Morris as "this is a locale where we might do some of the things which we are reluctant to do in this country". 13 The sort of "things" referred to may, in our view, be inferred from a memo Wakeham wrote to Cullman the same year in which he stated "Let's face it. We are interested in evidence which we believe denies the allegation that cigaret smoking causes disease".14 However he concluded that this would be difficult, if not impossible, so instead he proposed three alternatives. One was to conduct research for other causes of smoking-related diseases, to get the industry "off the hook", although "prospects for a positive benefit are small". A second was to establish "expert scientific witnesses who will testify on behalf of the Industry",14 although he noted that it might not be long before such witnesses were tainted by association with the industry. The third, which he favoured, was to undertake research to discover information of direct use to the industry on biological, psychosocial, and epidemiological aspects of smoking.10

Although INBIFO was 100% owned by Philip Morris after the transaction, it appears that the company was reluctant to be connected too closely with it, arranging its acquisition through a Swiss subsidiary so that "In this way our involvement would not be unduly exposed".13 As a consequence, in a confidential document from 1972, a complex system of communication between the two was established. This involved the appointment of a coordinator, Ragnar Rylander, to act as an interface.15 Rylander's main employment has been at the University of Gothenburg, Sweden, for most of the time that he acted in this capacity. The relationship is summarised in a diagram drawn by Philip Morris (figure). Rylander was at that time at another Swedish university and had previously undertaken assignments for both Lorillard (another tobacco company) and Philip Morris. He was to be "officially . . . carried on the books as a consultant to FTR [Fabriques de tabac réunies, a Philip Morris

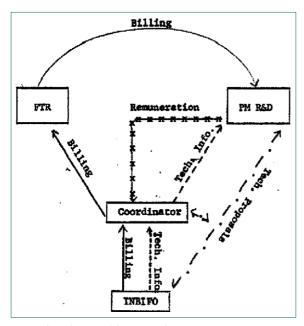


Figure: Relation between Philip Morris and INBIFO
FTR= Fabriques de tabac réunies, a 100% subsidiary of Philip Morris, based in
Neuchâtel, Switzerland. PM R&D=Philip Morris Research and Development.
Coordinator=Professor Rylander. Source: reference 15.

subsidiary] and would be paid by FTR".16 This arrangement apparently minimised any formal connection between Philip Morris and INBIFO, even though it was clearly stated in the confidential document that any proposals for studies would only be authorised by Philip Morris, with the co-ordinator simply being informed of the decision. Rylander's approach to the relation of tobacco and health appears to be indicated in a later report by Shook, Hardy and Bacon, a law firm with close links to the industry, which states, in relation to a workshop that he was organising:17 "Dr. Rylander prepared a brief memorandum 'for internal use only' concerning the workshop. His major point was that he did not feel that the workshop could or would be in a position to give environmental tobacco smoke a 'clean bill of health'. However, Dr. Rylander did believe that he could bring a healthy scepticism to the conference and some of the claims being made about environmental tobacco smoke." Further information on Rylander's extensive links with the tobacco industry over the following three decades can be found http://www.prevention.ch/rylanderpm.htm.

Other documents appear to reveal the reason why having a "separate" organisation might be desirable. Thus, a request for an analysis of a new flavour formula in 1976 included the statement that "We may want to maintain confidentiality over the results; therefore, thought should be given to the use of INBIFO". Another memo contained the statement that "We are still anxious to keep confidential the fact that INBIFO has done its own glycerol inhalation study."

However it is our view that the clearest description of INBIFO's place in the Philip Morris structure came from declaration of Ian Uydess, a former Philip Morris employee, in 1996.20 He had worked with Dr Tom Osdene, who was Professor Rylander's contact point at Philip Morris. He described how "I subsequently found out (by asking around) that hardly anyone [at Philip Morris] knew anything about INBIFO ... I also remember hearing that on occasion, some of the results and/or initial observations from some of Dr Osdene's programs were being communicated verbally, rather than in writing . . . All in all, it seemed as if there was an 'inner company' within Philip Morris that conducted at least some of its investigations 'behind the scenes' on a strict 'need-to-know' basis. Interestingly enough, many (if not all) of these activities appeared to be related, in one way or another, to these sensitive topics of 'smoking and health". He continued "I was convinced that some of these groups/individuals may not have even known that they were being used as the 'extended resources' of this 'inner company'". However he also gave evidence that this arrangement was known about by selected senior executives in Philip Morris' headquarters.

The sensitivity of the relationship can also be gathered from a memo from 1977, in which a senior Philip Morris executive reprimanded a researcher in Philip Morris' Swiss research centre for suggesting that samples might be sent directly to INBIFO. He wrote "This suggested procedure is in direct conflict with our communications from the New York Office. We have gone to great pains to eliminate any written contact with INBIFO, and I would like to maintain this structure. Therefore I am advising ... to continue sending samples to Neuchatel [a city in Switzerland, in which FTR are based] for transhipment to INBIFO. If this procedure is unacceptable to you, perhaps we should consider a "dummy" mailing address in Köln [Cologne, in Germany, the location of INBIFO] for the receipt of samples. The written analytical data will still have to be routed through FTR if we are to avoid direct contact with INBIFO and Philip Morris USA."21 He then requested the researcher to retrieve all copies of his original letter.

Further insights can be obtained from a hand-written note, identified subsequently in court documents as having been written by Dr Osdene, which set out procedures to be followed in communicating within the system. These included "OK to phone & telex (these will be destroyed)", and "If important letters or documents have to be sent please send home—I will act on them & destroy" (the word "important" was underlined).

So what was INBIFO doing that Philip Morris was so concerned to distance itself from? There are two sources of information that give insight into this question. The first is papers published by INBIFO. Those published until 1998 can be found in a list of the Institute's publications.<sup>24</sup> An analysis of the titles suggests a difference in the periods before and after 1990. Between

1972 and 1989, 53 papers are listed, of which eight (16%) mention tobacco, cigarette, lung cancer, or nicotine (in various languages). This may seem somewhat surprising given that a 1990 report stated that about 80% of INBIFO's work was for Philip Morris, with 20% for its subsidiary, FTR, with 1-5% for other clients.25 However, between 1990 and 1998, 48 of 76 (63%) papers mention these terms. It is our view that one explanation might be linked to the fact that, in 1990, when concerns were beginning to be raised about potential disclosure of industry documents in American court cases, Philip Morris sought an opinion from Shook, Hardy and Bacon as to whether any documents held in INBIFO would be immune from discovery.25 They were advised that they were not and so could no longer rely on legal protection for their work although, as a subsequent document indicated, a detailed precautionary review of document holdings at INBIFO was conducted to identify any material on environmental tobacco smoke. However Philip Morris's lawyers seemed to draw some reassurance from the practice of all product reports prepared by INBIFO being returned to it after being reviewed by Philip Morris and most of its records being on computers and in German.26

There also appears to be a difference between some of the reports produced by INBIFO for internal use and some of those that were published in the scientific literature. In the 1980s INBIFO conducted a large number of animal experiments on sidestream smoke.

From the very beginning, those experiments showed the highly toxic nature of this type of smoke. For example, one INBIFO report sent to Philip Morris at Richmond, Virginia, via Rylander, in 1982, describes in great detail the results of exposure of rats to sidestream smoke.<sup>27</sup>

The findings seem quite clear and consistent. "All rats showed general signs of exhaustion after the end of the daily exposure. In contrast to the rats of the mainstream group, which recovered by the next morning, the rats of the sidestream groups continued to show shaggy fur and some pronounced respiratory symptoms characterized by whistling and rattling sounds" (page 1-6). "If one extrapolates from the experience of previous mainstream inhalation studies, the mainstream TPM [total particulate matter] concentration of this study would have to be increased by a factor of 3 to produce similar strong reactions than seen with sidestream exposure in this study" (page 1-14). "Additionally to the changes, seen with mainstream, sidestream-puffed or nonpuffed alike-caused more severe atrophic and necrotic leasons of the olfactory epithelium and frequent squamous cell metaplasia in the ciliated epithelium of the nasal cavity" (page 1-15).

A further report of this study<sup>28</sup> summarises the findings as follows: "The statistical evaluation of body and organ weights showed that tendentially sidestream smoke-exposed group with equal daily TPM dose react

stronger than the mainstream smoke-exposed group and the high sidestream smoke-exposed group react almost in the same fashion as the high mainstream smoke-exposed group, although the TPM concentration in the high sidestream smoke-exposed was approx. a factor of 4 lower than that in the mainstream smoke-exposed one" (pages 1–3) while another<sup>29</sup> states: "Sidestream smoke of the cigarette type 2R1 showed a higher toxicity in terms of body weight development, food consumptions, rectal temperature and respiratory frequency than mainstream smoke of equal TPM concentration. To reach the same effect on the mentioned bioassays with mainstream and sidestream smoke, the mainstream TPM-dose must be 2 to 4-fold higher than the sidestream TPM-dose" (pages 1–6).

The significance of these findings was emphasised in a letter written by Professor Rylander to Osdene: "The histology demonstrates more advanced lesions in the nasal epithelium and hyper and metaplasia in areas which are not affected by main stream smoke. The extent of cornification observed in these animals has never been seen before." <sup>30</sup>

Finally, an important role for INBIFO seemed to be to undertake experiments that could then be repeated by others, although "independently", knowing what the results would show, as illustrated in the comment "The result of such work has enabled us to provide accurate input . . . as to what could be expected to be seen in the Bruene experiment and led us to recommend that he support its conduct by the VdC [Verband der Cigarettenindustrie—German Cigarette Manufacturers Association]."<sup>31</sup>

By contrast, several of the published papers where the contact address listed for authors is INBIFO seem to fall into the third option identified by Dr Wakeham, providing information that is useful to the industry. The one epidemiological study listed in PubMed from this facility invoked an association between lung cancer and drinking green tea.32 This had many of the characteristics of, and involved some of the same authors, as the studies commissioned by the industry to suggest alternative explanations for the observed association between passive smoking and disease.33 Others cast doubt on the value of cotinine $^{3+36}$  and certain DNA markers<sup>37</sup> as measures of exposure to tobacco, a key issue in research on environmental tobacco smoke. A third group conclude that the substances commonly added to cigarettes are non-toxic. 38,39 However, in recent years, a few papers have been published that do seem to be looking at the mechanisms of tobacco-induced harm,40 albeit involving many of the same scientists as in some earlier activities such as the, now discredited, Centre for Indoor Air Research.41

The researchers at INBIFO do not appear to have published a single paper on sidestream smoke until 1994. This was confirmed in a letter from INBIFO to Shook, Hardy and Bacon<sup>42</sup> and we believe it can be

interpreted in the light of a 1989 statement that "Except for one brief presentation to the ETSAG [Tobacco Industry Environmental Tobacco Smoke Advisory Group] on one of the INBIFO experiments no one knows anything about our SS [sidestream] work, particularly within PM."31 However we have been able to trace more than 800 scientific reports dealing with sidestream smoke undertaken by INBIFO between 1981 and 1989. Even after 1994 they did not appear to have published their important findings on the dangers of sidestream smoke, even though it is likely that these would, almost certainly, attract considerable interest from prestigious journals. Yet, for reasons that are not entirely clear, one senior Philip Morris executive wrote to two other senior scientifically qualified executives in 1997 "I need your support in ensuring that ETS studies conducted and completed at INBIFO are submitted for publication in peer reviewed scientific journals" and then identified particular studies whose "submission and publication are of critical importance".44

As this correspondence shows, even the detailed analysis in this paper is, of necessity, incomplete, and many unanswered questions remain about precisely what the tobacco industry knew, and when, about the hazards of second hand smoke.

The tobacco industry documents reviewed in this paper allow the story of INBIFO to be told largely through the words of those most closely involved in it, and require little further comment. It is our view that they show how Philip Morris initially avoided any involvement with research that might possibly tell it what was already widely accepted by the scientific community, that smoking was harmful. When, eventually, senior executives were persuaded that the company required capacity to undertake biological studies, the initial business case appears to have concluded that this should be an in-house facility, in the USA. Yet further reflection apparently identified the danger of such a relation as it would make it difficult to deny knowledge of any findings generated, a key element of the industry's strategy. The availability of a functioning facility in Germany, with an established record of co-operation with the company, appears to have settled the matter. However, in what is our view an arrangement that is intended to ensure deniability, an arrangement was established by which a Swedish professor would act as an intermediary between INBIFO and Philip Morris. Stringent measures appear to have been employed to maintain the secrecy of these arrangements, extending to consideration establishment of a "dummy" mailbox and the dispatch of documents to the home address of a senior Philip Morris scientist where they would be acted on or destroyed. The arrangements appear to have been kept secret from many working within Philip Morris. The existence of this relation does, however, appear to have been known to certain senior executives.

The documentary evidence suggests that INBIFO maintained two quite distinct profiles. One, revealed in its internal reports, appears to have involved a very large programme of inhalation studies, some of which, as long ago as 1982, showed that sidestream smoke was more toxic than mainstream smoke, a key finding that could have informed the debate about passive smoking. We have been unable to find any evidence that these studies have been published. In contrast, its public image arose from the papers published in scientific journals. Many of these appear to be of considerable value to the industry, casting doubt upon the value of markers of passive smoking and suggesting alternative explanations for the observed epidemiological association between passive smoking and lung cancer.

It is our view that these internal documents demonstrate how Philip Morris was, contrary to its contemporary public statements, aware of the greater health risks posed by sidestream smoke from the early 1980s. However, the company appears to have chosen not to publish this even as it was conducting research to refute emerging evidence about the dangers of passive smoking.

What are the implications of these findings? It might be thought that, while an interesting historical account of the workings of the tobacco industry, it simply confirms what most people already suspected. Some Philip Morris executives have now testified under oath about the relation between the company and the facility, going so far as to describe it as the leading centre for inhalation studies in the world.44 Unfortunately, as revealed in responses to a recent, highly controversial paper on passive smoking,45 it appears that the industry's efforts to prevent further bans on smoking in public places continue unabated. As recently as April, 2002, Philip Morris, in an American court, rejected the statement that environmental tobacco smoke causes disease.46 In these circumstances we believe that it is essential to have a more complete picture of the evidence that goes well beyond what the industry has felt it useful to publish.

More generally, we also believe that it is essential that those involved in reviewing evidence on smoking and health should be aware of what appears to be the selective nature of what is eventually published by some scientists with links to the industry, and the evidence that sometimes mechanisms appear to have been used to disguise these links. Any research in this field must involve full disclosure of competing interests and any involvement of the tobacco industry in the instigation, design, analysis or interpretation of findings. Specifically, Philip Morris should be required to explain why it took the steps documented here to maintain what appears to have been considerable secrecy about its role in research on the effects of sidestream smoke and consequently its knowledge of its effects, effects that appear at odds with its public statements.

Looking ahead, the next goal of the tobacco industry is thought to be production of a "safer" cigarette. This appears to be consistent with some of the more recent research being produced by INBIFO. This work is unlikely to attract support from governments or foundations and we believe that it is likely to remain the preserve of industry-funded scientists. It is essential that there can be confidence that what reaches the public domain is the whole truth, and not a carefully selected subset of it.

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## Conflict of interest statement

PAD is president of OxyRomandie, a Swiss-based association for the prevention of passive smoking, which receives subsidies from the local government; JCR is physician-in-charge of CIPRET-Genève, an organisation responsible for smoking prevention financially supported by the local government; MM's work on tobacco control is supported by the National Cancer Institute, US National Institutes of Health, grant number 1 R01 CA91021–01. Following the release of a press statement by two of the authors (PAD and JCR) in Geneva in 2001 relating to Ragnar Rylander's conduct and links with the tobacco industry, Rylander took legal action against PAD and JCR alleging libel. MM appeared as a witness in the case. In December, 2003, the Geneva court found the statements by PAD and JCR, some of which are the subject of this paper, to be true. Full details of the legal process, including judgements, can be found at http://www.prevention.ch/rylanderpm.htm.

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