

THE BIRTH OF IARC

ATS-UNIS d'Amerique



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It is rare, in the history of nations, that one finds good reasons to render homage to the generosity and altruism of governments and those in power: the birth of the International Agency for Research on Cancer presents one of those rare occasions. – Lorenzo Tomatis

> Great things are done by a series of small things brought together. – Vincent Van Gogh

AN IDEA – NOVEMBER 1963

It is often difficult to identify the origin of an idea, good or bad. However, in the case of IARC one can reasonably conjecture that its conception was a result of the pain of loss associated with the disease it was created to combat. A single letter from a bereaved husband, relating the suffering of his wife after a cancer diagnosis, troubled the editor of the recipient newspaper and spurred him to action. In turn, his compassion, character, and connections, combined with the optimism of the times, generated the momentum for change. These small individual acts, triggered by emotion and empathy, resulted in an international political response resonating with shared experience across nations.

The letter was written by a journalist based in Nice, Yves Poggioli, a friend of the editor and a fellow member of the Movement for Peace, an organization formed in France after the Second World War. His personal loss triggered efforts from the end of February 1963 to create an international centre to fight against cancer that would be financed by taking resources directly from national budgets destined for nuclear armament. Poggioli approached several different organizations and individuals, including the French government, but with little response. In early April 1963, he approached the newspaper editor, asking him to forward this idea to the World Peace Council, another organization working for nuclear disarmament.

The editor receiving the letter was exceptional in several ways (see "Emmanuel d'Astier de La Vigerie – liberation from the burden of cancer"). Emmanuel d'Astier de La Vigerie was a Frenchman of aristocratic background, born in Paris in the first week of the 20th century. D'Astier attended the French Naval Academy but in his mid-twenties resigned and turned to a mix of journalism, poetry, and opium. A reflective dilettante, he began drifting increasingly to the political left, leaving behind his earlier monarchist tendencies. During the first months of the Second World War, d'Astier re-enlisted in the French Navy. After the fall of France in June 1940, his desire to do something to resist the occupation led to the formation of one of the three major resistance groups in the unoccupied southern zone of the country. The group, initially based in Cannes and called La Dernière Colonne, later moved to Clermont-Ferrand, subsequently changing its name to Libération-Sud.



Emmanuel d'Astier de La Vigerie played a central role in engaging the support of General de Gaulle for a new international cancer research agency.

EMMANUEL D'ASTIER DE LA VIGERIE – LIBERATION FROM THE BURDEN OF CANCER

It is no exaggeration to say that Emmanuel d'Astier de La Vigerie was a major public figure in the second half of the 20th century in France. Intriguingly, however, there seems to be little awareness of his key role in the creation of IARC. Of the several books written by or about d'Astier, none mention this episode. Perhaps this is because after his early engagement the baton was passed to other players, notably Antoine Lacassagne and Eugène Aujaleu, who took the initial idea and ran with it. Nevertheless, it is hoped that the current volume will shine a light on the remarkable legacy of d'Astier's initiative, whereby he built on the original impetus from Yves Poggioli.

D'Astier was a man who fundamentally had hope in humanity, a man who believed in people. He was also a man of action. Indeed, he spoke of ideas being insufficient if divorced from action. This resonates with his compassionate response to the letter from Poggioli and his direct approach to the head of state for a solution.

D'Astier was born on 6 January 1900, the youngest of eight children. It seems fair to say that he first found his purpose during the Nazi occupation of France in 1940. D'Astier had an overwhelming conviction to restore the dignity of France, and he turned that idea into action by creating the resistance movement Libération-Sud, along with Édouard Corniglion-Molinier (in La Dernière Colonne), Jean Cavaillès, and Lucie and Raymond Aubrac, among others. Bernard (d'Astier's undercover name) would later say that the friendships he made during that period could never be matched.

While the resistance movement would be the pivotal period in the life of d'Astier, first he had to free himself from his addiction to opium. Here again one sees a remarkable strength of character as he locked himself into a hotel room alone for several days until the desperate cravings had passed. He would later recount that having survived that pain, he had an inner confidence that he would not divulge information, even under the most severe coercion, should he ever be captured.

D'Astier first met General de Gaulle in mid-May 1942 in London. It was during a later visit to the British capital that he wrote the lyrics for the iconic song "La complainte du partisan". After the war, with the continued publication of the newspaper *Libération*, he had support from and associations with the French Communist Party. In 1950, d'Astier was one of the signatories to the Stockholm Appeal calling for an absolute ban on nuclear weapons. After the war, President de Gaulle invited him to be the French ambassador to the USA. It says something of d'Astier's strength of character and independence that he refused and focused on his writing, journalism, and a decadelong term as a far-left deputy for Ille-et-Vilaine in the French Senate.

In detailed interviews, d'Astier acknowledged the impact on him of closing his newspaper *Libération* at the end of 1964, describing himself as being at a "crossroads" and speaking of the "large hole" left in him by the closure. The proposal for an international agency may have been one of a series of creative ideas sparked by his search for new causes and meaning. The closure of *Libération* was about one year after the initial approaches to de Gaulle, but it would certainly have been weighing on d'Astier over that period. What is known is that on 23 October 1963, just two weeks before the open letter to de Gaulle on 7 November, d'Astier had received a friendly and personal letter from de Gaulle commenting on his most recent book (*On Stalin*). In the 1960s, d'Astier was also to unexpectedly call for voters to support de Gaulle in elections. Therefore, the relationship between the two men was most certainly alive and rather positive during this time.

After the closure of *Libération*, d'Astier had fresh projects afoot. He launched a new publication, *L'Evénement*, notably with the participation of a young doctor called Bernard Kouchner, who would later establish Médecins Sans Frontières and would also serve as French Minister of Health. But d'Astier was to reach his widest audience by presenting a 15-minute weekly television show dealing with current affairs in the mid-1960s. D'Astier died of a myocardial infarction in 1969. Browsing through photographs of d'Astier, one is struck by the number in which he is seen smoking a cigarette. Sadly, he succumbed to the consequences of that habit, one of the risk factors for cancer to interest IARC throughout its history.

D'Astier was appointed Compagnon de la Libération, as were two of his brothers, Henri and François, although they each arrived there by different routes. On his own journey, somewhere along the way, in what may have been a mere footnote for this remarkable man, d'Astier lit the flame that has burned brightly in the form of IARC for the past 50 years.

D'Astier used his journalistic background to give shape to Libération-Sud, distributing tracts calling on the population to resist both the occupying forces and the Vichy government. This dangerous activity evolved into the production of the underground newspaper *Libération*. The first edition appeared in early 1941, and publication continued after the war until November 1964. This was the newspaper that the grieving man wrote to, acknowledging that d'Astier used *Libération* to fight for political causes and peace but challenging him: "What are you doing against cancer?" D'Astier later wrote of how the letter weighed heavily on him. The spirit of resistance was to turn its sights on a new enemy.

If this correspondence was one key element leading to the proposal of d'Astier to create an international cancer agency, another was certainly his wartime connections. Libération-Sud was part of the eventual unified French resistance movement, which evolved into the National Council of the Resistance (Conseil National de la Résistance). In this unification process, d'Astier met with Jean Moulin (later captured by the Gestapo and imprisoned and tortured in Lyon), the emissary of General Charles de Gaulle, in exchanges that, famously, were not without disagreement. D'Astier subsequently participated in the evolving leadership coalescing around de Gaulle, meeting with him in both London and Algiers. These activities opened doors for access

to other political leaders, including a meeting with Winston Churchill in which d'Astier forcefully made the case for the United Kingdom to provide arms for the French resistance. In 1944, d'Astier briefly served as Minister of the Interior in the provisional French government.

Calling on the president

Given d'Astier's direct involvement with de Gaulle from the earliest stages of the war, it is perhaps no surprise that he looked to the president to champion the idea of an international effort to combat cancer. The prior relationship opened doors that might otherwise have remained closed. D'Astier made two documented approaches to de Gaulle – the first alone, and the second through an open letter with the support of 12 leading French public figures (see "Co-signatories to the open letter").

The first meeting, in July 1963, appears to have elicited limited interest from de Gaulle. D'Astier said, "De Gaulle listened. I don't know if he heard me." The exception was when d'Astier presented the big idea

to fund the initiative, as proposed by Poggioli: an appeal to the major nuclear powers to donate a small percentage of their defence budgets to the new international agency. De Gaulle raised a heavy eyelid and asked a few questions. He did not say yes or no. D'Astier left feeling naive and without much hope.

The second approach revolved around the open letter, which was delivered to the Élysée Palace on 7 November 1963, with copies to the embassies of the Soviet Union, the United Kingdom, and the USA. It was signed by d'Astier and 12 co-signatories (two unnamed people had refused to join the list) from diverse fields of expertise. Some of these individuals were also received by de Gaulle at the Élysée. The co-signatories included the noted cancer expert Antoine Lacassagne, who had retired from the Radium Institute in Paris but was president of the French League Against Cancer (see "French friends – Antoine Lacassagne"). Indeed, it was after discussions with Lacassagne and a cancer biologist, Marcel Bessis, that the letter was formulated. D'Astier noted that the project took shape at the end of a "summer of rotten weather". It is true that the summer in France was unseasonably cold and wet that year - perhaps the additional time indoors helped the planning process.

CO-SIGNATORIES TO THE OPEN LETTER

These 12 leading French public figures from different disciplines co-signed the open letter of Emmanuel d'Astier de La Vigerie to General de Gaulle:

Louis Armand (Engineering) Pierre Auger (Physics) François Bloch-Lainé (Finance) Ambroise-Marie Carré (Clergyman) Jean Hyppolite (Philosophy) Antoine Lacassagne (Oncology) Charles Le Corbusier (Architecture) Pierre Massé (Civil Engineering) François Mauriac (Journalism) Francis Perrin (Physics) François Perroux (Political Economy) Jean Rostand (Biology) - LE MONDE - 8 novembre 1963 - Page 13

ACTUALITÉS MÉDICALES

Pour développer la lutte contre le cancer c des personnalités françaises lancent un appel en faveur d'une institution internationale de recherche pour la vie

Des savants, des écrivains, des sociologues, ont lancé un appel pour que les Etats-Unis, l'U.R.S.S., la Grande-Bretagne et la France assurent le financement d'une institution internationale de recherche pour la vie. En voici le texte, qui, en France, revêt la forme d'une requête au président de la République :

sances, qui actuellement reconnaissent la nécessité de la coopération internationale pour resoudre certains problèmes humains, de faire un geste immédiat et raisonnable au profit d'une stratégie universelle pour la vie. Il s'agit de mettre tout en œuvre pour parvenir à une mobilisation contre un des l'humanité : le cancer.

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- Malgré certains succès thérapeutiques déjà importants, il n'y aura pas de victoire décisive sur le cancer tant que ne seront pas déterminés la nature du mal et le mécanisme de sa production. La victoire sur le cancer sera une grande victoire de l'homme.

- Un prélèvement dérisoire sur le budget des grandes puissances permettrait de mettre sur pied une institution internationale de lutte pour la vie, sous le contrôle effectif des organismes qualifiés de l'O.N.U. et des savants cancèrologues les plus incontestés.

- Les soussignés soulignent qu'une réduction d'un demi pour cent sur les budgets militaires des Etats-Unis, de l'U.R.S.S., de la Grande-Bretagne et de la France R.P. Carce, Jean Hyppolite, Antoine (réduction qui ne saurait modifier l'équilibre des puissances et qui pourrait être éventuellement conqu'une réduction d'un demi pour

. Les soussignés demandent aux sentie par d'autres puissances migouvernements des grandes puis- litaires) permettrait de multiplier par milliers le nombre des laboratoires, des chercheurs et des expériences. Ainsi seraient dégagés les moyens d'une stratègie universelle de la recherche sur la vie. Il ne suffit pas de congrès, de communications, de rencontres de discipline à discipline ; il faut un centre où puisse s'élaborer cette plus grands fléaux qui pesent sur stratégie universelle qui s'impose.

 A l'institution serait confiée par ailleurs la tâche d'informer dans un langage simple, mais très exact. des progres accomplis dans la recherche. L'opinion mondiale serait ainsi conduite à participer à une recherche et à un combat qui la concernent.

» Si les quatre chefs d'Etat des puissances désignées consentaient ce prélèvement dérisoire, le terme d'une victoire sur le cancer pourrait être avancé de nombreuses années.

- Nous nous adressons à la plus haute autorité de notre pays pour qu'elle donne en cette matière l'initiative à la France. -

A copy of the open letter to de Gaulle, published on 8 November 1963.

This open letter called for a "derisory" 0.5% of the military budgets of France, the Soviet Union, the United Kingdom, and the USA to be invested in an international cancer institution under the auspices of the United Nations and engaged in a "fight for life". The levy would not change the balance of military power, it was argued. The letter to de Gaulle also specified the insufficiency of conferences, communiqués, or interdisciplinary meetings; rather, a centre was needed where this universal strategy could be realized. There was positive press coverage of this proposal for a common international effort against cancer - "one of the greatest scourges weighing on humanity", as the letter put it. Here, one imagines that d'Astier's press contacts were brought into useful play. Typical was the New York Times headline of Friday 8 November 1963: "Use of Arms Funds on Cancer Is Urged".

The open letter to de Gaulle made little attempt to veil military parallels in this period of postwar reflection, arguing that if the heads of the four designated powers agreed to this proposal, then "the victory over cancer could be advanced by many years". Undoubtedly the pacifist was appealing to the general through analogies to wartime, when earlier cooperation might have saved many lives. A later press report, from October 1964, supports this view, with the French

Minister of Public Health and Population, Raymond Marcellin, mentioning that a peaceful cooperation among the major world powers could create an atmosphere favourable towards atomic disarmament of all nations. The letter was certainly about cancer, but it was also about disarmament and peace.

In fact, a more general backdrop of antinuclear sentiment is discernible behind the positive proposal for an international cancer centre. For example, Poggioli initially contacted d'Astier because of his links to the World Peace Council, an organization initiated by the Soviet Union to promote peace campaigns around the world.



Antoine Lacassagne was a leading figure in the French cancer community in the 20th century, after originally receiving his medical training in Lyon.

FRENCH FRIENDS – ANTOINE LACASSAGNE

Born in the Loire in 1884, Antoine Lacassagne was undoubtedly one of the most influential of the 12 French co-signatories who joined Emmanuel d'Astier de La Vigerie in sending the open letter to General de Gaulle in November 1963. Indeed, Lacassagne was the only cancer expert among the 13, and in a subsequent French newspaper article d'Astier spoke of discussions with Lacassagne before composing the letter to de Gaulle. No doubt the nascent ideas of d'Astier were complemented by the technical expertise and experience of the highly respected Lacassagne.

Lacassagne stayed involved as the idea took form, and he was present at the first of the government meetings, in December 1963, where the idea of a new cancer research organization was really developed. While celebrating his 80th birthday, he served as a vital link between the French government and the academic conference organized by UICC in Stockholm in 1964. Lacassagne appears to have walked this particular tightrope between the scientific and political worlds with some considerable aplomb.

There were strong links to Lyon as well. No evidence has been unearthed to say that Lacassagne's loyalty to Lyon played a role in the selection of the city for the new IARC headquarters, but it is fair to speculate that he would have supported the idea. In fact, Antoine Lacassagne's father was a professor of legal medicine at the Faculty of Medicine and Pharmacy in Lyon. Antoine, in turn, was a doctor of medicine and intern in the Lyon hospitals. He stayed in Lyon until his mentor, Claudius Regaud, moved to the Radium Institute in Paris, alongside Marie Curie, and called

Antoine to join him. After serving in the medical corps in the First World War, he would spend the rest of his career at this famous centre, building on his training in pathology and playing a pioneering and leading role in radiobiology and X-ray treatment of cancer. He was eventually succeeded by Raymond Latarjet and upon retirement became president of the French League Against Cancer, a position he occupied until his death in 1971.

It is perhaps notable that after his retirement in 1954, Lacassagne was one of the invitees to the first conference of the Pugwash Movement, working for peace and against weapons of mass destruction. The proposal to redirect military funds towards cancer research must have resonated deeply with Lacassagne, as it did with other key players in this new venture, including Yves Poggioli, d'Astier, and Alexander Haddow.

The first president of the World Peace Council was Frédéric Joliot-Curie, a physicist who had worked on the nuclear chain reaction before the war and was married to Irène Curie, the daughter of Marie Curie. At the World Peace Council, Joliot-Curie worked with d'Astier. Both were recipients of the Stalin Peace Prize (later renamed the Lenin Peace Prize), the Soviet equivalent of the Nobel Peace Prize. Joliot-Curie, who died in 1958, had close links with the nuclear physicist Pierre Auger, who was later to sign the open letter to de Gaulle along with d'Astier.

REPLY FROM GENERAL DE GAULLE

General de Gaulle responded within two days to the open letter from d'Astier and his co-signatories.

Mon cher Maître,

L'idée de promouvoir la recherche sur le cancer au sein d'une institution internationale procède d'une inspiration généreuse et je considère comme souhaitable que la France s'y intéresse.

Il me paraît, en effet, conforme à ses traditions qu'elle s'engage dans une œuvre où se retrouve une triple vocation : la coopération entre les peuples, le progrès de la condition humaine et l'avancement des sciences.

Aussi ai-je confié au ministre de la santé publique le soin de prendre toutes les initiatives nécessaires à cet égard.

Je vous demande de le faire savoir à toutes les personnalités signataires avec vous du message qui m'a été adressé et vous prie de croire, mon cher Maître, à mes sentiments fidèlement dévoués.

Ch. de Gaulle

My dear Sir,

The idea of promoting cancer research in an international institution draws on a generous inspiration, and I consider it desirable that France participate in it.

It seems, in fact, consistent with its traditions that France should engage in a work where three aspirations can be found: cooperation between peoples, the improvement of the human condition, and the advancement of science.

I have therefore asked the Minister of Public Health to take all necessary initiatives in this regard.

May I ask you to make this known to all the public figures who co-signed with you the message that was sent to me, and I beg you to accept, my dear Sir, the assurances of my deepest respect.

Ch. de Gaulle

It is unclear why this second approach made the difference to de Gaulle. It is known that around this time he made an unannounced visit to his personal physician at the Gustave Roussy Institute in Paris, a specialist cancer centre, before he died from the disease. In any event, de Gaulle replied positively and with remarkable swiftness (see "Reply from General de Gaulle"). In his letter of 9 November 1963, the president acknowledged the idea as motivated by generosity, and he highlighted three features that remain at the heart of IARC to this day: cooperation between peoples, improvement of the human condition, and advancement of science.

Entry on the scene of the World Health Organization

On 11 November, four days after the publication of the open letter, Marcellin, the responsible French Minister, was on the telephone to the Director-General of the World Health Organization (WHO), Marcolino Gomes Candau. Marcellin requested a meeting within 48 hours in Paris – a meeting that took place on 13 November. From a modern-day perspective, one can only look with wonder on such pace and decisiveness. There is anecdotal evidence that the call from Marcellin to Candau came with the message to meet anywhere, anytime, to discuss a project for a cancer institute funded at the level of about US\$ 1 million per day. Marcellin also contacted the Federal Republic of Germany and Italy, informing them of de Gaulle's desire to see them join this venture. One can appreciate the idealism behind a cooperative health-oriented venture between the Federal Republic of Germany, France, Italy, the Soviet Union, the United Kingdom, and the USA less than 20 years after the end of the Second World War.

Marcellin delegated the follow-up to his Director-General of Public Health, Eugène Aujaleu, who was present at that first meeting with Candau (see "French friends – Eugène Aujaleu"). Aujaleu would end up playing a major role in the creation of IARC. By chance, he had also been in Algiers when the Allies arrived in 1942 and as a result became responsible for public health within the provisional French government. After the liberation, Aujaleu was nominated to the role of Director of Social Hygiene within the Ministry of Health, and he represented France at WHO from the late 1950s until the early 1980s. This experience at WHO no doubt helped him in piloting the idea of a new cancer agency through the complexities of the WHO administrative procedures. Indeed, it is Aujaleu who chaired the preparatory meetings before consideration of the plans by the World Health Assembly.

In retrospect, one is struck by the remarkable flurry of activity and momentum, born perhaps of broad alignment of two fine ideals: the desires to fight for peace and against cancer. At heart, one can detect a humanitarian response to a recognized burden on the human condition. There was a natural justice in reducing the resources assigned to one perceived scourge to increase those available to tackle another. However, this idealism was soon to meet the twin pillars of bureaucracy and self-interest, with a risk that the project would be abandoned or so watered-down as to be hardly noticed.

FRENCH FRIENDS – EUGÈNE AUJALEU

Eugène Aujaleu was born in 1903 in the Tarn and Garonne. Having studied medicine in Toulouse, he focused on infections and was appointed to a chair in epidemiology at the Val-de-Grâce Hospital in 1936. At the outbreak of war, he directed the services of hygiene and epidemiology of the French Armed Forces. Finding himself in Algiers as the Allies landed, he played a major role in establishing the health services in the liberated regions, resulting in 1943 in his appointment to head the Public Health and Assistance Services in the provisional French government, under de Gaulle and alongside d'Astier.

Aujaleu appears repeatedly in the transformation of IARC from idea and idealism to reality. He was "the man from the Ministry" who used the systems and processes of the World Health Organization (WHO) to good effect, leading to resolution WHA18.44 in May 1965. He was the primary contact for the discussions about IARC within the Ministry of Public Health and Population, where he had been named Director of Social Hygiene in 1944. In 1956 he became the first Director-General for Health, contributing to major reforms in medical education and the creation of the French university teaching hospitals.

Aujaleu also had a foot firmly in WHO in his role as representative of France from 1948 to 1982, which was recognized by awarding him the Léon-Bernard Foundation Medal. In fact, it was Aujaleu who presented the case for the new



Eugène Aujaleu played a central role in piloting the creation of a new cancer research agency through the administrative hurdles of national governments and WHO. Here, Aujaleu (right) is pictured with former WHO Director-General Hiroshi Nakajima.

cancer agency to the World Health Assembly and, following that success, it is no surprise that he was the chair of the first IARC Governing Council meeting, in September 1965. In the mid-1970s, he appears again, this time bringing clarity to the different evolving roles of IARC and WHO in relation to cancer research and control, writing an important report on the topic in 1977. Aujaleu was the first Director-General of the French Institute of Health and Medical Research (INSERM), from 1964 to 1969, a position he therefore took up over this period of IARC becoming a reality and establishing its home on French soil.

FROM CONCEPTION TO BIRTH - NOVEMBER 1963 TO MAY 1965

The 18 months from the time of the open letter to de Gaulle in November 1963 through to the adoption of a resolution to create IARC at the World Health Assembly in May 1965 was a period when idealism met pragmatism. Concerns were voiced as different scientific players, both within France and further afield, considered the potential impact of a new, well-funded international organization, and governments considered the proposed level of financing. Various suggestions for the new organization were formulated. These included the idea of an institution that would coordinate global research by sharing out research tasks internationally, or would serve as a conduit for distribution of funds to existing research institutes.

No doubt some of the concern among the cancer research community in France and elsewhere resulted from a chronic lack of funding within existing centres. The United States National Institutes of Health (NIH), for example, was causing concern as it reduced its spending on health research abroad; in 1963, the total NIH expenditure in more than 50 countries amounted to US\$ 13.5 million. Throughout, one can sense an inherent tension between wanting to capture the potential benefits of a (relatively) massive influx of much-needed funding for cancer research and wishing to avoid the creation of a new organization that would be the sole or major beneficiary of those funds. Linked to this was the fear that such a well-funded centre would draw all the best researchers away from national institutes.

The World Health Organization

WHO was taken by surprise by the scale of the French proposal and had to consider how this might affect the ongoing planning of its own research activities. No doubt the initial contact between the French president and the WHO Director-General was vital to the explicit support that emerged quite early in the process. Furthermore, history reveals a close working relationship and mutual appreciation between Marcellin and Candau.

In parallel, WHO was going through "a radical reappraisal" of its role in research. It so happened that in the second half of November 1963, just after the open letter to de Gaulle, two crucial meetings of scientific advisers were already planned in Geneva: one to specifically consider the role of WHO in cancer (a cancer unit had been created in 1959), and another to plan a broad and ambitious World Health Research Centre with three divisions – epidemiology, biomedical research, and communications science and technology – and with a staff of about 1300 people. It is probably not insignificant that the pre-eminent British epidemiologist Richard Doll was present at both discussions.

The nascent idea of a World Health Research Centre was discussed at the Seventeenth World Health Assembly, in 1964, and more meetings took place over the following year, before a further debate at the Eighteenth World Health Assembly, in 1965. However, it became evident that given the ambition of the project, the WHO Director-General "would be frustrated in his desire" to see this new centre come to fruition.

In addition, by that stage the "de Gaulle initiative" for a cancer research centre was firmly on the table. In fact, one can note many planned features for the World Health Research Centre that would later characterize IARC: for example, the division of epidemiology was to conduct laboratory research to study health and disease patterns in different countries, the biomedical division was to study mechanisms of action relevant to cancer and other major biomedical problems, and training was to feature prominently.

It appears that at the World Health Assembly in 1965, the idea of a broader health research centre became reality on a more modest scale in the form of IARC. The creation of IARC may have salvaged something of the aborted centre for the WHO Director-General while also encapsulating cancer research opportunities identified by WHO. In fact, WHO was already involved in several international studies – notably on comparisons of lung cancer in Norway and Finland, breast cancer in seven different parts of the world in relation to lactation and childbearing, and cancers of the buccal mucosa in India and the Central Asian republics of the Soviet Union – as well as prominent activities in the international classification of human tumours via a wide set of pathology reference centres globally.

Certainly, Candau must have been strongly supportive of the new cancer agency for such rapid progress to have been made through the WHO administration as well as the formal debates and resolutions at the Seventeenth and Eighteenth World Health Assemblies. Evidently, the support of Marcellin and Aujaleu was also unstinting. Strategic considerations around the creation of a new organization seem to have coalesced with a vision for the scope of activities of such an entity. Those in influence were handed not just an outline sketch of a new structure but a painting of what it would achieve if realized.

Another international cancer organization

There was already an international cancer organization, which had been in existence since 1933: the Union Internationale Contre le Cancer, or in English, the International Union Against Cancer (UICC, now called the Union for International Cancer Control). It was not unexpected, therefore, that UICC also had to consider the potential impact of the French initiative.

The first to act was the eminent professor Alexander Haddow, director of the Chester Beatty Research Institute in London and president of UICC from 1962 until 1966. Haddow wrote supportive letters to the heads of state of the five countries considering de Gaulle's proposal, while pointing out the need to consider the idea in the light of current and planned activities by existing organizations. Haddow informed de Gaulle about the letters and sent him, as an example, the one written to United States President Lyndon B. Johnson. De Gaulle's reply to Haddow is particularly striking because, while he acknowledged the efforts of UICC and others, he focused on the need of researchers to work together if the victory over cancer is to be won, referring to "a union of research workers that extends beyond national frontiers". He clearly wanted more than a loose exchange of information among cancer researchers. This recognition was insightful and influential as the conception of an international organization gave birth to IARC. UICC continued to debate, both internally and externally, the shape and form of any new organization, with varying degrees of enthusiasm. In late 1963, Haddow expressed his anxiety at how things were developing to both Candau and Marcellin. There seem to have been two major concerns, aside from consideration of the direct impact on UICC activities. The first was that WHO would not be the best home for a research centre, both because of the heavy bureaucracy and because of its predominantly public health orientation (UICC initially considered the priority for the new centre to be basic research). The second was that as the scale of the likely investment began to shrink from the original bold vision of the levy on defence budgets, UICC favoured the strengthening of existing research efforts rather than the creation of a new but small centre, which might be ineffective.

LE GÉNÉRAL DE GAULLE

Monsieur le Président,

Je vous remercie d'avoir bien voulu m'exprimer les espoirs que vous mettez dans les récentes initiatives que j'ai cru devoir prendre **a**u nom de la France,

La lutte contre le cancer me semble être l'une des missions les plus hautes qui puisse s'imposer aux chercheurs de notre temps. Je n'ignore pas les généreux efforts de l'Union Internationale dont vous assurez la présidence. Je n'ignore pas les brillantes recherches dont vous avez honoré la Grande-Bretagne. Il me semble, cependant, que la victoire sur le cancer ne pourra être assurée que par une union des chercheurs par de-là les frontières. Dans cet effort commun, je vous remercie de l'aide que vous nous apportez.

Veuillez croire, Monsieur le Président, à mes sentiments les plus distingués et les meilleurs.

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Monsieur Alexander HADDOW, President International Union Against Cancer,

President de Gaulle wrote to the president of UICC, emphasizing the need for something more from the new initiative than was available in existing organizations.

To develop a purely scientific view, UICC organized an international conference in Stockholm on 7–9 September 1964 and invited world-leading cancer experts to consider alternatives by which the new organization might take form. This gave rise to some tension with WHO, possibly creating the impression of a battle for control of the initiative. Haddow, in his opening remarks and commenting on the original vision of the French initiative, stated: "As a Scotchman the idea appealed to me immensely, offering great benefits for no more expenditure than we had already agreed to spend. Its failure thus far I greatly regret as a person, since in England I am much involved with questions of peace and disarmament; but in practice this idea or ideal certainly appears to be dead."



Leading cancer researchers discussed the "French initiative" at the UICC conference in Stockholm on 7–9 September 1964.

Haddow, a participant in numerous disarmament initiatives, was visibly disappointed by the rupture of the link between reduced military budgets and increased cancer research funding. This is consistent with the recollection of Jean-Francisque Delafresnaye, then the UICC chief executive, who remembers Haddow having forcefully voiced displeasure at the proposal for a much scaled-down initiative during the second meeting of the participating governments, held seven months earlier in Paris; UICC was not invited to subsequent planning meetings by the participating governments.

Varying degrees of freedom

In retrospect, one can trace two different visions during this period. The first one, among the cancer research community, was focused more on what a new organization might do and leaned towards the creation of a completely independent organization, either intergovernmental or nongovernmental, outside of WHO. The second vision, among the five interested governments in liaison with WHO, was focused on how to create the new organization as intergovernmental but in relations with WHO, either as an arm of the organization or linked via a signed convention, allowing the new organization to benefit from the administrative infrastructures and avoiding the need for a completely separate development. In retrospect, the fact that the initiative was at the very highest level in France, promoted by the French Minister, and had the personal support of the WHO Director-General, was decisive. Ultimately this position within WHO and the broader United Nations family has been at the root of IARC's unique contribution, providing an independence to conduct and coordinate international collaborative research and a status, as the cancer agency of WHO, to lend impact to its findings and pronouncements.

Aujaleu, working on the WHO model, was concerned, however, as to how decisions would be made on research projects if approval was needed by the 100 or so WHO Member States, and whether cancer might

be diluted in the wider health remit of the parent organization. He also felt that countries would be more likely to support an autonomous and less impersonal cancer-focused organization. Several possible solutions lay within the WHO Constitution, and the one chosen was via Article 18(k), which allowed the World Health Assembly to create institutions to promote and conduct research. Presumably this would have been the route selected to create the larger World Health Research Centre had it materialized. In any event, as Aujaleu perfectly expressed it, the solution delivered an organization that was both independent and included within WHO. It was a far-sighted solution.

These early, chaotic, occasionally fractious days resulted in important consideration of how the new organization would offer something different, avoiding duplication with existing efforts nationally and internationally. UICC, in turn, was to become one of IARC's long-standing and valued collaborators in several areas, not least capacity-building.

Towards a resolution

Two key technical meetings were held in Paris before the World Health Assembly in June 1964 to formulate plans for the new organization. The first, on 17–18 December 1963, was attended by representatives from the Federal Republic of Germany, France, the United Kingdom, and the USA (the Soviet Union was invited but did not attend) and by the WHO Director-General and the president of UICC. Lacassagne was present as one of the French delegation, providing the link back to the original co-signatories of the letter to de Gaulle. The meeting was called in a hurry, occurring just one month after the open letter was sent, and as a result there was relatively limited time for preparation. The meeting did, however, outline areas of potential activity, including a cancer information centre, tumour classification, epidemiology, and training and support for researchers worldwide by provision of standards and resources for projects. By all accounts the meeting was preliminary in nature but positive.

At the second meeting, held on 27–28 February 1964, the same participants as well as observers from the United Nations Educational, Scientific and Cultural Organization (UNESCO) debated different governance models and drew up more detailed plans, which were eventually summarized in a document to the World Health Assembly. By this time governments had had the time to formulate their positions, and some of these had become less than wholehearted in their support. Interestingly, one sees emerging a name, the "World Research Agency for Cancer", and the idea of Governing and Scientific Councils with a Secretariat, which would include technical experts and operate in close liaison with WHO. The proposed plans were remarkably similar to the final governance structure of IARC. The Governing Council was to be the "supreme authority of the Agency".

It was also at this February meeting that the crucial issue of budget was considered in detail for the first time. Sadly for cancer research, military leaders were going to sleep a little easier in their beds, even as the war in Viet Nam raged. A calculation across the six countries (the Federal Republic of Germany, France, Italy, the Soviet Union, the United Kingdom, and the USA) of 0.5% of military expenditure yielded the stunning annual sum of US\$ 396 million (presumably the origin of the "US\$ 1 million per day" budget that Marcellin had relayed to Candau). Of this sum, US\$ 265 million was to come from the USA and about a tenth of that amount from the United Kingdom. It is perhaps not surprising, therefore, that a counterproposal came from the USA, delivered by the head of the delegation, Assistant Surgeon General James Watt. This included a budget based on a flat rate of US\$ 100 000 per country, well short of an annual budget of US\$ 1 million and, somewhat symmetrically, less than 0.5% of the original vision. It is here that Haddow reportedly used strong language to emphasize that the American proposal bore no resemblance to the idea put forward by de Gaulle. To the surprise of some, the French delegation nevertheless agreed to use the American draft governance document, including the budget, as a basis for further discussion.

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A post hoc analysis of the financial model of 0.5% of defence budgets redirected to cancer research (prepared by A.G.B. Sutherland, head of the Unit of Administration and Finance at IARC in the late 1960s and early 1970s).

These two Paris meetings in December and February resulted in a resolution of the World Health Assembly on 19 June 1964 authorizing the WHO Director-General "to enter into discussions with the countries concerned with a view to the establishment and operation of a World Research Agency for Cancer." The proposal to the World Health Assembly had been made by Aujaleu on behalf of the governments of the Federal Republic of Germany, France, Italy, the United Kingdom, and the USA. The deal was not done, but the die was cast.

Places, names, and dollars

After the World Health Assembly in 1964, a meeting was held at the Ministry of Foreign Affairs in Paris on 27 July 1964. France remained determined to see the project come to fruition despite the change in the financial model. From this meeting one can see the first notes about the possible location for the new organization. Several interested French cities had come forward to the Ministry, but two favourites emerged: Vaucresson, on the outskirts of Paris, near the Raymond Poincaré Hospital in Garches, and Lyon, "because of the proximity to Geneva, where WHO is located." Lyon was ready to provide an entire building in the Brotteaux district as a temporary solution and was even able to make available "within 48 hours" a large office in the wings of the City Hall itself. Although further preparatory meetings did take place in Paris on 29 September–2 October 1964, the next series of detailed discussions was held in Lyon the following year, perhaps a further indication that the home of the new organization was to be this former capital of Roman Gaul, once known as Lugdunum.

The intergovernmental meetings in Lyon comprised three sessions, on 16–18 February 1965. Discussion turned back to the budget, and a prolonged debate ensued. The participants, chaired by Aujaleu, were trying to balance five individual countries paying an annual contribution of a maximum of US\$ 150 000 each with the recognition that a total of US\$ 750 000 would be a modest start indeed. In fact, the immediate concern was that the scientists tasked with advising on the new agency's programme later the same year might consider this too small a sum to be worth turning up to discuss!

Harold Himsworth from the United Kingdom proposed one way out of the conundrum: to send invitations to 10 more countries to join the new organization, arguing that with 15 countries the total annual budget would be about US\$ 2 million. Candau suggested that this sum should be adopted as a starting point to aid the scientific planning, and this was eventually the agreed position from the meeting. There was also discussion as to whether to seek additional countries in time for the looming World Health Assembly. The group did not wish to be exclusive but recognized the difficulties for countries to take decisions in the short time that remained. There is an interesting reference to the Netherlands, present at the meeting, which had been deliberating participation for five months. The Netherlands would eventually become an IARC Participating State two years later.

The discussion of names also continued, no doubt partially influenced by the different mother tongues of the discussants. The name "World Research Agency for Cancer" had disappeared. The proposed French

version of the name now included "centre international", with the English translation, used by the Brazilian WHO Director-General, being literal: "international centre". Himsworth from the United Kingdom made a case for "international agency" because this would be more expansive, the word "centre" implying "activities in one place". This concept is consistent with earlier comments from Lacassagne, who had reportedly spoken of an international institution and not an international institute, which in French would also have been more limited than the broader collaboration desired. The outcome of this debate is reflected in the difference between the names in English and French, persisting to this day, whereby both "agency" (in English) and "centre" (in French) were deemed to imply something more than work performed in a single place. This breadth was never meant to be interpreted as there being no need for a headquarters and core staff, but rather it pointed towards the anticipated degree of international participation by national scientists in the work of IARC. This principle is also illustrated by the fact that IARC Participating States should not only contribute financially but also participate in research through the collaboration of their scientists. By 19 February 1965, Aujaleu was writing letters of invitation to the first Scientific Committee meeting in which he referred to IARC by its permanent names, in both French and English.

Interestingly, one name that didn't end up associated with IARC was that of the recently assassinated United States President John F. Kennedy. The suggestion of attaching the late president's name to IARC had been made by Pierre Massé, one of the co-signatories of d'Astier's letter to de Gaulle, and also in the original letter of Haddow to President Johnson in late 1963, but does not seem to have been pursued further.

Scope of activity

The work now moved to a new phase: specifying what the new agency would do. Discussions in Lyon on 30 March–6 April 1965 were based on a series of working papers coming from meetings held earlier in Geneva: on a cancer research information centre (Working Group meeting held 3–5 February 1965), epidemiology (14–16 December 1964), pathology (14–18 December 1964), and training (undated, but at least partly drafted by Albert Tuyns, later to become one of the first IARC scientists).

The scientific advisory committee, comprising 12 outstanding cancer researchers from across the world, met on 30 March–2 April 1965, highlighting what could be learned through an international collaborative dimension and the value of training. Epidemiology was identified as a principal sphere of activity, including studies on the occurrence and patterns of cancer. It is noteworthy that the three participants in the epidemiology subgroup were Richard Doll, John Higginson, and Daniel Schwartz, who was the head of the first cancer epidemiology unit in France, at the Gustave Roussy Institute.

The Scientific Committee emphasized that epidemiologists should not work in isolation, and thus pathology was highlighted as of importance, in relation to epidemiology. There were also areas that are not today a part of IARC's work, notably comparative oncology among domestic, farm, and wild animals as well as a role in

the distribution of well-characterized animal strains and other research tools for experimental studies. The indicative budget of US\$ 2 million was considered a minimum if the new agency was to make any impact on a world scale. The budget constraints led to the scientific experts placing less emphasis on some areas, including the possibility of a global information centre on cancer research.

Immediately after the scientific meeting, the government representatives met on 3–6 April and were joined by the chair and the rapporteur from the previous days' events: Otto Mühlbock from the Netherlands and Richard Doll, respectively. The emphasis on epidemiology was supported, as was training, but the relative lack of resources directed to the cancer research information centre was not universally appreciated. The point was reiterated for the new agency to avoid duplication with national centres and to conduct research that such national centres could not accomplish. There was also a view that the agency would support research in national centres, including by funding studies. This is manifest in one form via the Collaborative Research Agreements that IARC establishes with collaborating centres across the world.

In terms of budget, France continued to fight hard for higher contributions, first arguing for US\$ 400 000 per country, based on the Scientific Committee's views, but later dropping to US\$ 200 000 in an attempt to reach consensus. In the end, agreement could only be reached on US\$ 150 000 from each of the five countries present, with the hope that more would join. A 5-year budget was set on this basis, although subsequently IARC moved to budgets set on a biennial cycle. Aujaleu "trusted the Agency would soon be endowed with funds larger than they had been able to vote at the present meeting so that the hopes raised by its creation would not give way to disappointment." There was also the intention that this "core" budget would be supplemented by additional resources for specific projects.

World Health Assembly resolution WHA18.44, of 20 May 1965, formally creating the International Agency for Research on Cancer.

WHA18.44 Establishment of an International Agency for Research on Cancer

The Eighteenth World Health Assembly,

Cognizant of Article 18 of the Constitution which provides, *inter alia*, that one of the functions of the Health Assembly shall be to establish such other institutions as it may consider desirable, with a view to promoting and carrying on research;

Considering that the Governments of the Federal Republic of Germany, France, Italy, the United Kingdom of Great Britain and Northern Ireland, and the United States of America have agreed to sponsor the creation and to participate in the functioning of an International Agency for Research on Cancer¹ in accordance with the provisions of its Statute;

Considering that many governments have expressed their interest in the creation of such an Agency; and Considering resolution WHA17.49 of the Seventeenth World Health Assembly,

DECIDES to establish an International Agency for Research on Cancer which shall carry on its functions in accordance with the provisions of its Statute (annexed).

Handb. Res., 7th ed., 1.7.6; 1.11

Twelfth plenary meeting, 20 May 1965 (Committee on Programme and Budget, sixth report) Aujaleu made the positive point that equal financial contributions from the different Participating States would avoid the risk of policy being dictated by a few countries that paid far more than others. A relatively small difference in scale of financial contributions among IARC Participating States has been a model retained over the past 50 years, achieving exactly the outcome anticipated by Aujaleu. Incidentally, true to its original ideal at least, France was the only country to take its initial financial contribution to IARC from its defence allocation.

The culmination of this remarkable roller-coaster ride, from a simple letter through to a proposal to the World Health Assembly for the creation of a new international agency for research on cancer, finally came to fruition in May 1965.

THE BIRTH OF IARC – MAY 1965

IARC's birthday can be considered to be 20 May 1965, when the World Health Assembly passed the remarkably brief and perfunctory resolution WHA18.44 creating an agency for international cooperation in the field of health under Article 18(k) of the WHO Constitution. Technically, however, WHO announced on 20 September 1965 that IARC had begun to function on 15 September 1965 upon confirmation by the five named Participating States (the Federal Republic of Germany, France, Italy, the United Kingdom, and the USA) of their formal agreement to observe and apply the terms of the IARC Statute, attached to the World Health Assembly resolution. IARC began to take form.

Members of the first IARC Governing Council at the meeting in Lyon, which took place on 23 and 24 September 1965.



The Soviet Union was not among the founders of IARC but was one of the countries that soon joined. Higginson shared his memories about Nikolai Blokhin and how he persuaded Nikita Khrushchev to support the Soviet Union to join the Agency. – David Zaridze, former IARC scientist

The first meeting of the IARC Governing Council took place less than a week later, on 23 and 24 September 1965, with Aujaleu as the chair, accompanied by Giovanni Canaperia from Italy as the vice-chair. At that meeting, the Soviet Union was represented because it was one of the countries, along with the Netherlands, that had taken a close interest in the planning phase. Both Australia and the Soviet Union became

Participating States at that meeting, thus taking to seven those countries committed to IARC's development. In 1966 Israel also became a Participating State, perhaps through the participation of Isaac Berenblum from the Weizmann Institute of Science in the scientific planning meetings. The Netherlands joined shortly afterwards, in April 1967, and this group of Participating States was to steer IARC through the rest of the 1960s. By the time IARC moved into its own premises, in 1972, the number of Participating States had grown to 10; Belgium and Japan had joined, but Israel had withdrawn in 1971. The annual budget had reached US\$ 2.4 million, a little over the minimum amount envisaged seven years earlier.

The IARC Scientific Council met for the first time on 25 September 1965. The meeting was attended by a striking set of world cancer leaders, including Richard Doll, Abraham Lilienfeld, Nikolai Blokhin, and George Klein as well as Isaac Berenblum, demonstrating the importance with which this new international organization was viewed (see "The first IARC Scientific Council"). Indeed, Doll is widely known to have been approached when the discussion turned to the question of the first IARC Director, but he declined.

John Higginson took office as IARC Director on 1 July 1966 and started to build a small group of scientists around him. Among the first were Calum Muir, Albert Tuyns, Gregory O'Conor (seconded from the United States National Cancer Institute), Guy de Thé, Lorenzo Tomatis, Pavel Bogovski, and Walter Davis (from Haddow's Chester Beatty Research Institute). Higginson set many of the priorities for IARC that persist to the present day, including a firm commitment to the need for a strong interdisciplinary approach to understanding the causes and prevention

THE FIRST IARC SCIENTIFIC COUNCIL

Members of the first IARC Scientific Council, which met on 25 September 1965: I. Berenblum (Israel) N.N. Blokhin (Soviet Union) P. Bucalossi (Italy) W.R.S. Doll (United Kingdom) H. Hamperl (Federal Republic of Germany) B. Kellner (Hungary) G. Klein (Sweden) A.M. Lilienfeld (USA) G. Mathé (France) D. Metcalf (Australia) O. Mühlbock (Netherlands) P.N. Wahi (India) of cancer. Doll remained a strong supporter of IARC. He was unable to attend the opening of the new IARC tower building in Lyon in 1972, writing to Higginson, "I am particularly sad as I have such a close connection with the Agency since the idea for it was conceived."

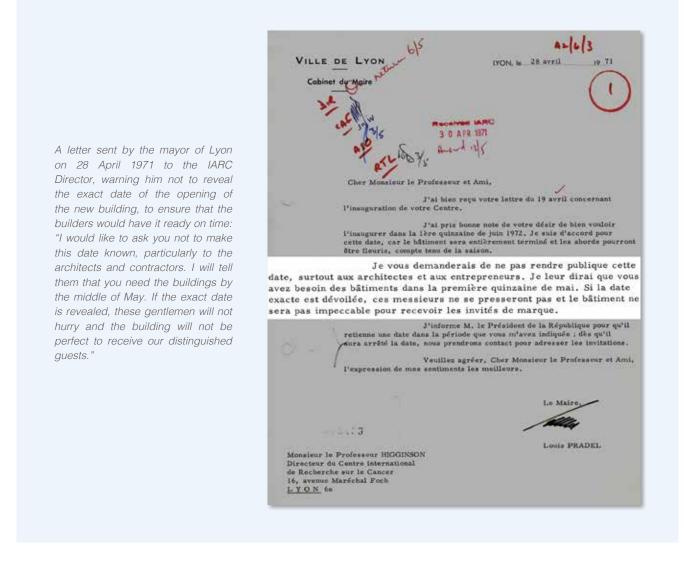
The first sentence of the IARC Statute, which accompanied resolution WHA18.44, stated: "The objective of the International Agency for Research on Cancer shall be to promote international collaboration in cancer research." The Statute also defined the governance structure, with both Governing and Scientific Councils. The WHO Director-General would be a member of the Governing Council along with each of the Participating States, but it would be the Governing Council that would set the programmes and budget of the Agency. The Governing Council would also select the IARC Director, who is the chief executive officer and is responsible to the Governing Council, not to the WHO Director-General. The Governing Council also decides which WHO Member States may become IARC Participating States. All of this added up to IARC being an autonomous agency within WHO, open to any WHO Member State that wished to participate both financially and through the contribution of its scientific experts; this is why IARC has Participating States, rather than Member States.

Those who gave form to IARC showed great skill in achieving the right balance between complete integration within WHO and absolute independence. They wanted the best of both worlds, and their vision has proven inspired. IARC is autonomous to a remarkable degree but is still part of WHO and therefore of the wider United Nations family. This solution has also enabled IARC to enjoy a distinct individuality in its external relations, developing its own reputation as a global leader in cancer research and in turn bringing great prestige back to WHO.

As a research agency with this degree of independence, IARC has been able to investigate difficult, often politically inconvenient topics and to present the science on which others can base policy actions. The lack of interference in that research process is testament to the adherence of Participating States to the principles on which IARC was founded 50 years ago. As a consequence, all concerned within the Secretariat and on the governing bodies carry a heavy weight of responsibility to maintain those principles into the future.

A PLACE TO CALL HOME

Where would IARC be located? France was the natural host country for this new international organization, and IARC remains – with UNESCO – one of only two United Nations organizations to be headquartered in the country. Lyon was formally confirmed as the new home for IARC, according to the official journal of the French National Assembly, at the first IARC Governing Council meeting, in September 1965. In his speech at the inauguration of the IARC tower building in 1972, President Georges Pompidou made reference to the strong tradition of medicine in Lyon and the proximity to Geneva and WHO headquarters as reasons for this choice. Aujaleu also noted that the geographical separation from WHO headquarters was another element in ensuring the autonomous nature of IARC.



The mayor of Lyon at the time, Louis Pradel, was also strongly in favour of Lyon being IARC's host city. Pradel was Lyonnais to the core, passionately committed to the city, and served as mayor from 1957 until his death from cancer in 1976. A hospital in Lyon carries his name, while the main general public hospital is named in memory of his predecessor, Édouard Herriot; perhaps these associations are further testimony to the great importance placed in Lyon on the pursuit of excellence in medicine and science, continuing and developing to this day. Pradel was also apparently a pragmatic man who understood human nature. His letter to the IARC Director, in anticipation of the grand opening of the new IARC tower building, provides one delightful example.

George Klein was a member of the first IARC Scientific Council, which met in 1965, and he participated in the planning meetings for the new agency. Klein recalls, "The mayor of Lyon spent a surprisingly large amount of time with us. It was quite clear that he wanted the new agency there. We were clearly impressed by Lyon and supported it as the site. During the subsequent years, we were impressed by the developments – the new building in particular – and it was our feeling that we had made a good choice."

Until May 1967, IARC was hosted by WHO in Geneva. A key date in its development was the signing on 14 March 1967 of the host agreement between WHO and France, permitting IARC to set up its Lyon



Premises at 16 avenue Maréchal Foch were made available to IARC by the City of Lyon from 1967.

headquarters. The mayor made temporary accommodation available at 16 avenue Maréchal Foch, with additional offices for biostatistics elsewhere in the city centre, and the official "opening" of IARC was fixed as 22 May 1967. As promised, IARC also had access to some of the fine rooms of the City Hall in Lyon, a magnificent building dating from the mid-17th century.

By this stage discussions had already begun on new, purpose-built accommodation; Pompidou visited Lyon on 24 March 1968, when he was shown the model of the new tower building. In the meantime, the local scientific and medical community was extremely supportive: laboratories were made available in the French Institute of Health and Medical Research (INSERM) and by the Mérieux Institute, and IARC was able to rent space from the Centre Léon Bérard with the support of Roger Sohier and Marcel Dargent, the director of this renowned regional cancer centre. Prefabricated buildings were also erected on the future site of the IARC tower to provide space for the laboratories, some offices, and animal housing facilities. These two-floor "temporary" buildings were to persist for more than 20 years. Even in the late 1980s they were still being used to house a small colony of rabbits for antibody production, as well as serving as the location for the French and English language classes – frequently at the same time!

The new IARC tower certainly made a statement. Particularly in the early 1970s, the 14-floor building soared above all others in the vicinity. The architects assigned by the City of Lyon were Pierre Bourdeix and Paul Guillot, and the consulting architect for IARC was Roland Mendelssohn, chief architect of INSERM, Paris. Even today in its ageing state the building can impress: on a bright Lyon day of clear, unclouded blue skies, the concrete pillars and blue fascia lead the eye soaring upwards while the solid, square design emanates presence and reliability. The entrance hall is enhanced by the sculpture in solid mahogany by Pierre Mathieu, representing the "triumph of life over the destructive elements of the environment" – a concept befitting the work of IARC and its many partners worldwide. As a footnote, IARC's address is 150 cours Albert Thomas, and one might note with a degree of irony, given IARC's origins, that Thomas was French Minister for Munitions during the First World War, later to make his mark as the first director of the International Labour Office.



On 23 March 1969, French Prime Minister Maurice Couve de Murville laid the first stone of the IARC tower building.

The first stone of the IARC tower building was laid by French Prime Minister Maurice Couve de Murville on 23 March 1969, and the building was inaugurated by President Pompidou just a little over three years later, on 9 May 1972. Pompidou was accompanied by his wife and no less than five French Ministers. At the inauguration, John Gray, the chair of the IARC Governing Council, emphasized that the work of the Agency "should be planned without regard to political and national boundaries." Pompidou spoke of the



need to remove the fear and myths surrounding cancer, and finished his address by stating, "Gentlemen, may the solidarity of mankind find in your work a broad scope of application and success."

There were messages of support from heads of government, notably United States President Richard Nixon, who had signed the National Cancer Act the year before with the famous declaration of a "war on cancer", and United Kingdom Prime Minister Edward Heath, a Europhile who had just led his country into the European Common Market.

President Pompidou addressing the audience at the inauguration of the new IARC tower building in May 1972. Behind him is seen the mayor of Lyon, Louis Pradel.



1.0 Bowning Street Whitehall

I PLEDGE THE STRONG AND CONTINUING SUPPORT OF MY COUNTRY TO ITS IMPORTANT VORK PD VE ARE GRATEFUL TO THE GOVERNMENT OF FRANCE FOR MAKING IT POSSIBLE FOR THE STAFF TO HAVE EXCELLENT PHYSICAL FACILITIES IN VHICH TO CONDUCT THEIR URGENTLY NEEDED STUDIES PARA SINCERELY PARA RICHARD NIXON PARA ROGERS

COL NIXON ROGERS

Many letters of congratulation were received from leading figures when IARC opened its headquarters in Lyon. Shown here are two examples, from United States President Richard Nixon and United Kingdom Prime Minister Edward Heath. I congratulate the International Agency for Research on Cancer on the occasion of the inauguration of the new Headquarters Building so generously provided by the French Government and the City of Lyon. Her Najesty's Covernment, in common with the governments of the other participating states, places the greatest importance on the fight against cancer and is eager to explore all opportunities for increasing international co-operation in this field. I am confident that the new facilities inaugurated today by President Pompidou will enable the Agency to continue and expand to the best advantage its contribution to cancer research.

Edward Jean

8 June 1972

A GROWING CONCERN

Over time, as IARC became established, some of the floors of the tower, originally unoccupied, were filled. Further expansion came with the opening of additional buildings and facilities. In 1988 the wealthy Japanese businessman and philanthropist Ryoichi Sasakawa made a donation to permit the construction of much-needed meeting rooms. The main new meeting room was named after Her Imperial Highness Princess Kikuko Takamatsu, who was well known and respected for her philanthropic activities related to cancer research.

An additional building was erected in 1994 to house the large cohort study of nutrition and cancer (the European Prospective Investigation into Cancer and Nutrition [EPIC]; see the chapter "Nutrition, metabolism, and cancer"), which included space for the liquid nitrogen tanks filled with several million straws containing biological specimens. An interesting addition to the IARC estate was the Latarjet building, named after Raymond Latarjet, which was opened in 2000 (see "French friends – Raymond Latarjet"). The front of the building, designed by Christian Drevet during the period when Paul Kleihues was the IARC Director, is

made to resemble DNA sequencing gels, capturing a time when that technology was at the cutting edge of cancer research.

The inherent structure of the early-1970s tower building did present a problem in the early 1990s, when unacceptable levels of asbestos were discovered. The building was closed for many months as a result, while specialist teams dealt with the expensive removal of this carcinogenic substance. It also resulted in the dispersion of IARC personnel to various sites around the city, for both office and laboratory accommodation, In the 1990s we had to evacuate the building because it was full of asbestos, which had been recognized as a carcinogenic substance. We therefore had to move to different buildings in town. It was a major operation, and I remember that very well. – Keiji Saita, former Director of Administration and Finance at IARC

recapturing something of the spirit of the late 1960s. Certainly the "crisis" represented another occasion when the local Lyon community proved its solidarity with the Agency and its global mission.

As evident from the opening sentences of the IARC Statute, collaboration was at the heart of the vision for the Agency. In the early years, this was also in evidence through the creation of several IARC Regional Centres, perhaps modelled on the much larger Regional Offices of WHO and a symbol of the vision that IARC should not be limited to a single physical location (see "The IARC diaspora"). IARC had such offices in Nairobi, Kenya, in Singapore, in Kingston, Jamaica, and in Tehran, Iran.



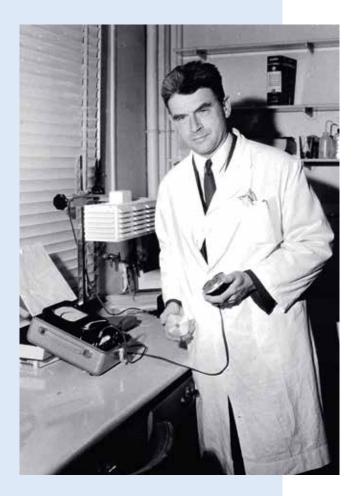
Ryoichi Sasakawa (centre) was present to open the Princess Takamatsu Hall in 1988 with the IARC Director Lorenzo Tomatis (right).

FRENCH FRIENDS – RAYMOND LATARJET

Born in Lyon in 1911, Raymond Latarjet was a fiercely proud Lyonnais and a major force in cancer research in France throughout the second half of the 20th century. His father was a professor of medicine, and he came from a family of surgeons. Remarkably, his first research was on the fluctuations in atmospheric ozone and the effect of ultraviolet radiation on living organisms – this was in 1935. He would go on to pursue his doctoral studies on the effects of ultraviolet radiation, and this background was probably one reason why Antoine Lacassagne invited him in 1941 to join the Radium Institute in Paris, where he started to take an interest in cancer.

After the end of the Second World War, Latarjet spent time in Cold Spring Harbor, USA, working with Salvador Luria. He conducted studies of mutations in viruses, consequent to irradiation, and they developed the renowned Luria–Latarjet curves. In 1954 he became director of the Biology Section at the Curie Foundation-Radium Institute, taking up the reins from his mentor, Antoine Lacassagne.

In 1959 Latarjet had a significant influence on the future of molecular biology in France through his participation in an advisory group on science reporting directly to the French president. His son, Francis, remembers him recounting many times a meeting in Paris with de Gaulle where there were 12 experts from many different leading areas of science, each



Raymond Latarjet in his laboratory at the Radium Institute in Paris.

given 5 minutes to make their case. De Gaulle listened to each presentation and explained the attraction that some of the great ideas that he could grasp intellectually, of exploring space or the ocean depths, might be expected to have for a politician in his position. However, he said, despite all he had heard, deep within "I ask myself if this mysterious molecular biology, about which I understand nothing and will understand nothing, ... might be the basis of a new medicine about which today we have no idea, but which could be the medicine of the 21st century." Molecular biology was selected as the top priority by the advisory group.

Raymond Latarjet was an outstanding clinician and researcher, but his interests extended far and wide. He was a well-respected alpinist, took part in Arctic exploration, and was a champion skier as a student. He was extremely knowledgeable about literature and music, and his wife was a professor of music at the Paris Conservatory. He was also a writer, winning recognition for his work in this capacity.

Latarjet was the chair of the IARC Scientific Council in 1972, and in the same year he was elected as a member of the French Academy of Sciences in the Section of Cellular and Molecular Biology. Given his Lyon affiliations, the Latarjet building, designed by the architect Christian Drevet, is a fitting reminder of his strong support to IARC over much of its early history.



The front of the Latarjet building.

The office in Kenya was synonymous with Allen Linsell, who coordinated IARC's early work on liver cancer (see the chapter "Carcinogens in the human environment"). The office in Iran was based on the interest in the high rates of oesophageal cancer in the Caspian littoral region (see the chapter "Nutrition, metabolism, and cancer"). Each centre was also linked to the development of cancer registries to describe the local cancer patterns.

These outposts of IARC, which were difficult to sustain, closed after a decision of the Governing Council in May 1980. However, an IARC office in The Gambia has been hosted by the United Kingdom Medical Research Council since the mid-1980s, linked

to the Gambia Hepatitis Intervention Study (see the chapter "Viruses and vaccines"). The office there was refurbished in recent years and has permitted many ancillary studies to be developed alongside the main project, which also resulted in one of the few population-based cancer registries in sub-Saharan Africa. The idea of regional centres has also been revisited with the recent establishment of IARC Regional Hubs for cancer registration within the Global Initiative for Cancer Registry Development (GICR) (see the chapter "Cancer registries: a worldwide endeavour").

Ramou Njie, head of the Gambia Hepatitis Intervention Study (GHIS) project, Tumani Corrah, director of the Medical Research Council (MRC) The Gambia, and IARC Director Christopher Wild at the opening of the refurbished GHIS offices on the MRC campus in Fajara, The Gambia, in 2012.



On arrival, the first thing I noticed was an enthusiasm and pioneering spirit. These people with a profile of "explorers" went into the field and had travelled the world, to Africa, Asia, and South America. At IARC there was this pioneering side but also a multicultural side, with Russians, Italians, Japanese, and so on, each having a different background. – Gilbert Lenoir, former IARC scientist

MAKING A DIFFERENCE

It is remarkable that within a decade of its creation, IARC was already well known internationally for its research. It had established studies on Burkitt lymphoma, oesophageal cancer, and liver cancer, among others, and had 10 Participating States and a budget in 1976 of US\$ 4.2 million. Senior scientists had been attracted to this new venture, with 150 people working together in Lyon from many countries across the world. IARC also had international visibility through

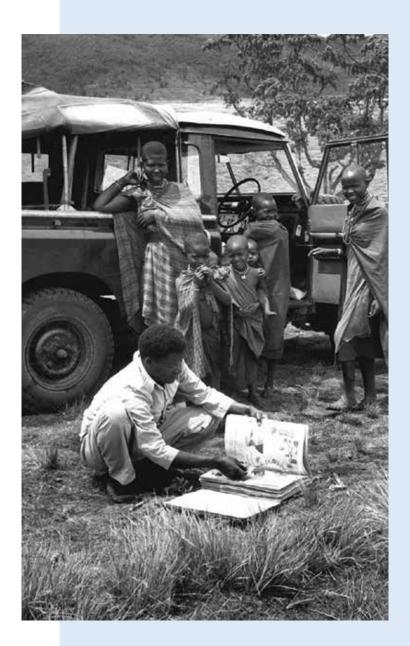
its Regional Centres. It had established laboratories in Lyon to study mechanisms of carcinogenesis and already had in place its renowned Monographs Programme to evaluate the evidence on agents thought to cause human cancer. In the first 10 years, the IARC Fellowship Programme had awarded more than 150 Research Training Fellowships to junior scientists and 200 Travel Fellowships to senior scientists.

This level of progress was no doubt due to the drive of those who came to Lyon to turn a vision into practical reality. But it was also due to the vision itself – a lasting belief that by joining together across national boundaries and focusing on improving the human condition, scientists can achieve much that is good.

THE IARC DIASPORA

The vision for IARC was always one of collaboration, acting as a catalyst to international research efforts. One approach was to have IARC Regional Centres in areas where the patterns of cancer were of particular interest and where data could be collected on the occurrence of possible risk factors. The purpose was to develop long-term programmes, with the location requiring a strong interest of the local research community, both scientifically and through provision of infrastructure support. These Regional Centres were also seen as venues where IARC postdoctoral fellows could conduct some of their research. IARC provided modest resources to support each office, for example on the order of US\$ 5000 annually, and the leadership was local.

One of the first Regional Centres was operational as early as 1967, in Nairobi, Kenya. The choice was partly based on the observations of high liver cancer rates in sub-Saharan Africa, coming soon after the discovery



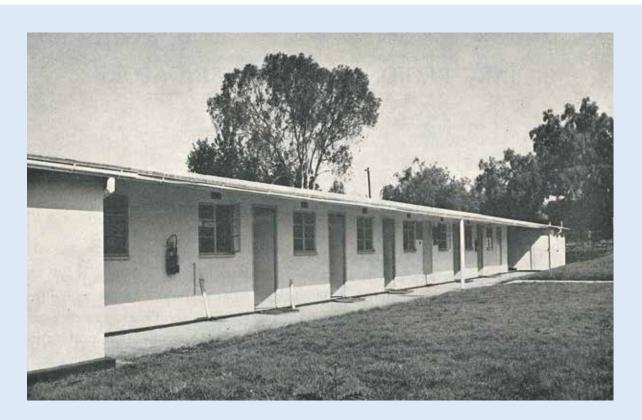
One of IARC's first studies, organized from its Regional Centre in Nairobi, was on aflatoxins and liver cancer in Kenya.

in the early 1960s of aflatoxins as the most potent naturally occurring liver carcinogens yet identified. The IARC Regional Centre in Nairobi would conduct many of the food analyses for aflatoxins in Kenya and in other countries such as Côte d'Ivoire, South Africa, Swaziland, and countries outside of Africa. Further work focused on Epstein–Barr virus and Burkitt lymphoma in collaboration with Guy de Thé, who had joined the scientific team in Lyon. The centre also played a role in supporting several cancer registries across the region.

The Nairobi Regional Centre was synonymous with the person of Allen Linsell, who was already based in Nairobi and worked tirelessly to have the centre established not only at a strategic level but also down to the details; at one point, he promised John Higginson that the required refurbishment of the premises would certainly "not exceed £400". Linsell oversaw the construction of buildings dedicated to this new IARC outpost and opened by Higginson in 1969, even before the IARC headquarters building in Lyon.

Linsell was joined in his research efforts on aflatoxins and liver cancer by Frank Peers and Gregory O'Conor as the investigations took shape, including the epidemiological studies in Swaziland of liver cancer, aflatoxins, and hepatitis B virus infection. The Nairobi Regional Centre was also involved in early experiments on aflatoxins in baboons as an animal model. Linsell would lead the centre for several years

before later moving to Lyon; in 1975, the leadership passed to Ambrose Wasunna, with continued financial support from IARC to maintain the office and research activities.



The new building of the IARC Regional Centre in Nairobi, opened in June 1969.



Ambrose Wasunna took over the leadership of the centre in 1975, after the departure to Lyon of Allen Linsell.

Singapore was another place chosen for an IARC Regional Centre – possibly the first, given that it was approved in late 1966 and formalized with the University of Singapore for an official opening in January 1967. As with Linsell in Nairobi, there was a key person involved in the developments, in this case Calum Muir. Muir was a pathologist working at the University of Singapore with plans to establish a cancer registry. Such a registry was lacking, but the enormous potential was recognized, based on the ethnic diversity, with the large populations of Malays, Chinese, and Indians having different cancer incidence rates. Interestingly, Muir would also later move to Lyon to join the growing complement of scientists helping shape the Agency.

The Singapore Regional Centre was established not least because of the commitment of Kanagaratnam Shanmugaratnam from the Department of Pathology, the person who would be the head of the centre for many years subsequently. The research studies focused on nasopharyngeal and liver cancers (including cholangiosarcoma) as well as on establishing the cancer registry, which began registration on 1 January 1968. The opportunities provided by the network of centres started to become evident, as Linsell linked up with the IARC Regional Centre in Singapore with respect to his liver cancer work in Nairobi.

The IARC Regional Centre in Kingston, Jamaica, was the third of those established by the end of 1967, in this case through an agreement with the University of the West Indies and under the responsibility of Gerrit Bras, a professor of pathology. The centre played an important role in supporting cancer registry development in Puerto Rico, Aruba, Bermuda, and Guyana, and also in Curaçao, where a high incidence of oesophageal cancer had been noted, with the disease at least as common among women as among men.

The IARC Regional Centre in Tehran was established somewhat later, in 1970, with the first formal agreement signed for the launch of the centre in 1971. Here, the major interest was also oesophageal cancer, with an extremely high incidence in the Caspian littoral region, where the rates in women even exceeded those in men. The work encompassed studies of opium use as well as other risk factors.

The formal agreement was with the Institute of Public Health Research at the University of Tehran, with the activities linked to the Babol Research Station. The agreement was maintained after the Islamic Revolution in the mid-1970s, but the work became more difficult to continue in practical terms. The Tehran Regional Centre was initially headed by E. Mahboubi through to the formal end of the agreement in 1980. In recent years, IARC has recommenced its work in the region, still without a firm conclusion as to the reasons for the startlingly high oesophageal cancer rates there (see the chapter "Nutrition, metabolism, and cancer").

The IARC governing bodies reviewed the Regional Centre model in 1980 and decided that the centres should be closed. Standard letters were sent out by Higginson to this effect, thanking the heads of the centres for their work and collaboration over the years. From then on, collaborations would be focused around projects, as opposed to programmes, supported by Collaborative Research Agreements. The collaboration with Singapore, for example, continued on that basis.