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THE FABBRICA DELLA PENICILLINA IN POSTWAR ITALY: AN INSTITUTIONALIST APPROACH

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SUMMARY

FABBRICA DELLA PENICILLINA IN POSTWAR ITALY

This paper focuses on the motives and long-term effects of the momentous decision to build a world-class biomedical research laboratory, the International Center for Chemical Microbiology, at the Istituto Superiore di Sanità in Rome, rather than develop domestic production of penicillin to meet the needs of a destitute postwar Italy. An institutionalist approach will provide a richer vision of the intersections of scientific and national political history in postwar Italy and the Cold War. The Center failed in its modernising mission due to an insular mentality producing an 'enclosure effect' against the State, the healthcare system and the pharmaceutical industry. The absence of a scientific base together with an economic policy of 'liberal protectionism' that placed premiums on import tariffs and the licensing of foreign products explains the path dependency of the pharmaceutical industry during the postwar years and its demise in the 1960s.

Introduction

The convoluted and contested history of the surge to world fame and quick demise of the 'fabbrica della penicillina' (the penicillin factory) at the Istituto Superiore di Sanità (ISS) in Rome has been recounted many times along different narratives. Traditional accounts represent the International Center for Chemical Microbiology into which the

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fabbrica was turned, as a watershed in the development of biochemistry and the origin of the Italian antibiotic industry[1]. Academic jealousy and obscure political machinations have been invoked to explain the sudden collapse of the empire the ISS's director, Domenico Marotta, had painstakingly built over a quarter of a century of uninterrupted 'iron-fist ruling under sweet manners'[2]. Some authors have associated Marotta's trial with a political plot against the new alliance between the Socialist and Christian Democratic parties of the early 1960s. A recent line of enquiry has connected the fall of Marotta to a common pool of 'occasioni scippate' (stolen opportunities) from Italy. Some scholars, however, have also begun to ground the fabbrica della penicillina and its main actors, Marotta and Chain, within their proper historical and institutional context[3]. Impeccable scholarly work has recently shown that both the traditional self-aggrandising narratives of 'commemorative practices' and the more recent 'paranoid style' of explanations of its fall, deflect attention away from an analysis of institutional causes and long-term after-effects[4].

Adopting an historical institutionalist perspective, this paper takes the fabbrica as a 'tracer' to examine the political negotiations and organisational and institutional reconfigurations that changed the original mission of the ISS and helped develop a new 'moral economy' of funding and managing research[5]. The steps of the Marotta affair are taken as a probe to unearth the controversies and justifications – prompted by the semi-private governance of the Center – surrounding new forms of practice and collaborations between its scientists and the industry. Finally, a brief outline of the effects on the Italian pharmaceutical industry will be provided.

Science and the fabbrica in early postwar Italy

Italy had emerged from the war a divided, debased and destitute country, where dire need clashed with governmental inertia[6]. Science and scientific research were deemed a luxury for better times; once

more pressing needs had been dealt with[7]. The short address given to the national assembly of the National Research Council (CNR) in 1946 by the Prime Minister, Alcide De Gasperi, was ambiguous enough to leave one puzzling over government policy for scientific research:

> *Today, the Italian people, burdened by worries and living in want and hardship, drag themselves towards the ascent of their renaissance. We don't have the means to help them feed themselves and to give them what to put on. It may seem ironic to talk to them about culture and scientific research.*

One year later, no ambiguity remained in the blunt reply that Vice President and Budget Minister, Luigi Einaudi, gave to an urgent request for money by the CNR president, Guido Colonnetti:

> *Our supreme duty is to put an end to the huge gap in the State budget and particularly to do whatever we can to prevent that, in order to bridge that frightful gap, we are obliged to the worst of means, that is to operate the press of the Bank of Italy…. a means that would bring the death of our economy and the dissolution of the State.*

How did it come about that the State funded an expensive cutting-edge research project at a time of financial austerity and dire need? How was it that Domenico Marotta was able to provide Ernst Boris Chain with the lavish world class research laboratory he had unsuccessfully pursued in England? Other health and research related public expenditures pale in comparison to the amount the Italian government spent on the fabbrica della penicillina[8]. Various sources put the final costs of the fabbrica between L 1.200 and L 1.700 million, with ad hoc payments of L 700 million. The 1947 health budget allocated L 250 million to consorzi antitubercolari, the state anti-tuberculosis community services, to combat one of the most pressing public health issues in postwar Italy. As for state-funded research, the budget for CNR over the years 1946, 1947 and 1948 was, respectively, sixty-four, 200 and 250 million liras.

Ambiguities, silences and misunderstandings about the goals of the fabbrica had lingered over its entire story, from the original idea in 1946, to 1961, when production eventually stopped. The initial offer from the United Nations Relief and Rehabilitation Administration (UNRRA) was unambiguous and the Italian government's intentions to build a State-owned plant to produce 'state-penicillin' followed suit. Who first suggested turning the production plant into a research laboratory is less clear. According to Clark, 'Marotta clearly had little idea of what was involved with the UNRRA donation' and, when Chain visited the Institute, 'most of its components were still unpacked'[9]. Chain advised Marotta that 'it was utterly uneconomical to put up the technically antiquated plant' donated by UNRRA, and that 'there was no case for the State to interfere with industry' in the distribution or selling of state-penicillin. However, Chain notes that 'I added that such a fermentation pilot plant would considerably strengthen the biochemistry department which he told me (emphasis added) he had the intention of organising'. According to Chain, Marotta was 'well aware' of Italy's backwardness in modern biochemistry, caused by her isolation during the autarky and the war. As a further argument in favour of a biochemistry department, Marotta pointed out that 'he had just succeeded in securing the services of the pharmacologist Daniel Bovet'. The strong position Chain took against a state factory is directly antithetical to the projects he had repeatedly submitted to the MRC and the Ministry of Health in the UK. In a detailed 1949 memorandum he envisaged 'a state-owned penicillin factory' in order to make the State 'independent of private enterprise for the supply of one of the most important and now frequently-used drugs in medicine' in order 'to produce this drug at lower cost'. Why Chain's advice to Marotta was so different from his plans in Britain is not obvious. Maybe, as Clark suggests, Chain had 'divided feelings' over what to do. Possibly Chain considered the capabilities and perspectives of the Italian pharmaceutical indus-

try to be inferior. Or perhaps he just decided to take from the many options he had at that time, the one which gave him the best chance of obtaining the massive outlay of money, manpower and materials needed to secure himself a place in the international world of antibiotics.

That the State gave Marotta in postwar destitute Italy what Chain had been denied in England demonstrates, as Bud suggests, 'Italian ambitions for a great future and their pride in a distinguished past contrasted with present poverty'[10]. This makes sense in a tense climate of the 'unjust' Paris peace and the nationalistic calls to an imagined past. It is also a tribute to Marotta's astute political manoeuvring: Chain repeatedly mentions the apparently unlimited funds which Marotta was so adept at conjuring up from the Italian government with bipartisan support from parliament.

When additional state financing was requested in order 'to improve and complete the production plant and upgrade its capacity to two hundred million o.u.', the special Health Committee of the Senate asked for explanations of past expenditure and the new request. The situation had changed since 1947, when the first instalment had been granted with no questions asked. Two private companies were now producing penicillin (and streptomycin) in Italy, providing the benchmarks expected from the ISS plant. A sceptical senator objected that the total expenditure for the fabbrica was now over one billion liras 'an amount at least equal, if not higher, than the cost of the private plants, which are not experimental and are at least twice as big as the ISS plant'. Objections were also raised to the generic justifications for the expenditure, which read 'to buy materials now lacking, part in the US, and part in Italy: 330 million liras; for a new electric power station: twenty million liras'. The use of the fabbrica was also called into question: 'what is this plant going to do? Sell penicillin at production costs? Compete with private companies? Will hospitals be asked or obliged to buy or use state-penicillin?'.

However, appeals to Marotta's scientific fame and personal reputation silenced the few dissenting voices. Parliamentary records report that on 22 February 1951 the president of the Senate Health Commission asserted that 'the decree has the seal of the most outstanding expert, the director of the Istituto Superiore della Sanità'. From the opposition benches, Senator Silvestrini of the Socialist party called for a vote of approval 'because the person running this Institute is a scientist of not just Italian but of world fame, professor Marotta'. Proposals for an 'inspection' or even an 'informal visit' to the ISS were quickly dismissed as a 'waste of time' when 'pressing problems' required a prompt approval of the funding. In addition, opposition parties supported the fabbrica as a dialectic weapon for their policy of placing the production of (at least) essential drugs under state control, analogous with the state's monopolistic production of quinine at the dawn of the century.

The crux of the matter is that the ambiguity was in the 'fabbrica' itself. What was called la fabbrica della penicillina actually combined industrial production with basic and technological research through the amalgamation of several multidisciplinary teams of over one hundred people, in genetics, fermentation techniques and technology, mycology, biochemistry and physics[11]. The kaleidoscopic activities performed by the International Center under the convenient shield and deceptive umbrella of the fabbrica della penicillina allowed them to claim whatever goal most suited funders' expectations. Of these, the production of penicillin was a sure failure. Gualandi, one of 'Chain's babies', frankly admitted that 'no one could qualify' the state production of penicillin as 'an economic and scientific success' and that 'the few tons regularly given to the Army and the Red Cross could have been bought for much less at market prices'. Production started in 1952, too late to help with the crisis caused by the US embargo on penicillin and streptomycin following the outbreak of the Korean War, and to successfully enter a market already crowded

with private firms – domestic and subsidiaries of US, French and British companies – overstocked with first and second generation antibiotics.

The Center, however, was also a world renowned scientific centre, attracting trainees and important scientists from all over the world and apparently reversing the brain drain which had been scattering Italian scientists since the inter-war years. In 1951, the Center was affiliated with the WHO program to 'stimulate the production of penicillin' in developing countries, with Chain chairing the WHO Expert Committee on Antibiotics, enhancing the reputation of the ISS and its director. In 1959, an article in *New Scientist* celebrating Ernst Chain, praised the Istituto Superiore di Sanità 'as a model of a smoothly run government organisation' and also 'a tribute to the administrative genius and personality of its director, Domenico Marotta'. Commemorative practices have boasted that the Centre 'resulted in the growth of the antibiotic industry in Italy' and paved the way for the development of Italian biochemical research. The Italian pharmaceutical industry did undergo an astounding expansion in the 1950s. However, this never included antibiotics produced by fermentation, a process too expensive for the capital-stripped Italian firms. In addition, without a solid scientific base, the industry underwent a sudden demise in the following decades. For these reasons, the momentous decisions that changed the mission of the ISS should be called into question.

Institutional forces and individual agency

Under the unpretentious title of 'Integrative norms on the organisation of the Istituto Superiore di Sanità' (Law 20 June 1952 n.724) the law approved just one year after the inauguration of the Centre, and issued in the very days the plant began production, stated that 'The Istituto Superiore di Sanità performs scientific research and produces sera, vaccines, antibiotic substances and other substances deemed

useful for its goals. It executes State controls, carries out investigations and fulfils all the other tasks entrusted by the law' (article 1). By prioritising research and making regulatory and control functions secondary, the law did more than just revamp the old dispute over the primary mission of the Institute, and necessitated more than just management of the clash between the Mertonian ethos of academically-inclined scientists and the shop-floor perspective of professionals in government labs. The new mission of the Institute brought to the fore institutional and personal conflicts of interest, which potentially hampered the capability of the ISS to shoulder its regulatory and control responsibilities in an expanding pharmaceutical market. The change in the institutional mission of the Istituto Superiore di Sanità from public health intervention and training to fundamental research was Marotta's lifetime masterpiece, which he had painstakingly pursued and crafted, step by step, as opportunities had allowed. In fact, Marotta's efforts followed an ironclad model, first explicitly revealed in 1942, but which can be traced back to negotiations between the Italian government and the Rockefeller Foundation in the early thirties[12].

The new ISS came out of the war unscathed, with its resources and manpower significantly expanded by its 1941 reform, and was by far the most important biomedical research institution in the country. However, its lavish labs looked 'rather empty' and 'devoid of original research' to the inquiring eyes of Ernst Chain. Marotta himself was well aware of the effects of the ten year-long isolation of Italian science during both the autarky and the war. He was also aware that the rise of 'big science', the increasing costs of doing research and the decline of public resources had made the traditional strategy of streamlining institutional funds for regulatory functions to boost his ambitious research projects grossly inadequate. Continuing the strategy that had worked so well with the fascist regime, Marotta used his personal influence and reputation with the government and par-

liament to obtain the huge state financial resources and the ad hoc regulatory adjustments which made the birth of the fabbrica della penicillina possible. Marotta himself mentioned the personal interest and active intervention of the Prime Minister, Alcide De Gasperi, in the securing of US funding for the fabbrica. Even more important was Marotta's shrewd political manoeuvring, which took full advantage of the continuity of the State[13]. Marotta proudly mapped his 'reference constellation' in his acceptance speech for the honorary degree in biology conferred by the University La Sapienza in October 1963, a few months before his arrest in April 1964[14]. He claimed a shared 'custom of life' with a long list of people with influential positions in the liberal and/or the fascist state, particularly in finance. The list was headed by Luigi Einaudi, President of the Republic, Governor of the Bank of Italy, Minister of the Treasury and the Budget and Vice President of the Council of Ministers in De Gasperi's third cabinet, who maintained the intellectual and material leadership of economic policy in the postwar years. Bonaldo Stringher had been governor of the Bank of Italy in the thirties and was mentor to Beneduce, governor in postwar Italy. And there was Luigi Rava, initially a Minister in the liberal state and then under Mussolini, and Thaon de Revel, war hero in the First World War and Minister of the Treasury with Mussolini, and many others, including Francesco Saverio Nitti and Vittorio Emanuele Orlando, who had been Prime Ministers in the liberal state and had been restored to influential positions in republican Italy. All of these were mentioned as 'life exemplars', 'mentors' and 'role models', from whom he had received 'tangible support' over the years.

Marotta's management of the Institute was therefore intensely politicised, as it depended on particular relationships with the government and parliament. This is where Marotta and Chain's otherwise similar attitudes toward the State and its bureaucracy possibly differed. Chain condemned 'the stultifying effect of government influence on

research' and attempted to become 'as independent as possible of both university and government financial support', securing private funds in order to escape 'the agonising experience of fund-raising every year'[15]. Opposed to both 'ivory-tower scientists' and 'oblivious industrialists', Chain was keen to see the boundaries between industry and the academy broken down[16]. Chain himself consulted for a number of companies and several governments around the world, which greatly contributed to his reputation as the 'major domo to the antibiotic industry of Europe'.

Chain's attitude certainly had an impact on changes in the governance of the Institute which slowly took place during the 1950s. In 1957, a bylaw allowed the staff of the Institute to provide personal consultancy to the same companies they were supposed to control and inspect. The semi-private research centres created on the side of the Institute and the Paternò Foundation for Scientific Research became the conduits for the money collected from industrial and public sources, including research grants and the royalties from patents developed by the Institute's staff. Parliamentary debates on the Marotta affair (see below) revealed that the Paternò Foundation, headed by Marotta, had acquired and licensed eighty-three patents developed by the Institute and managed close to L 200 million in grants that, according to Italian law, should have been routed through the Treasury. Fifty per cent of the royalties accrued to the Foundation was shared with the ISS staff.

The semi-private arrangements of the new governance of the ISS brought to the fore personal and institutional conflicts of interests. This was further compounded by its institutional regulatory functions towards the very same companies it was accepting donations from, selling licences to and providing with consultancies. Technical controls and inspections to register new medicines and authorise the officine farmaceutiche were delegated to the ISS. The ISS also had a key role in defining a 'standard' production price for the regis-

tered specialties. In addition, Marotta chaired the Commission on the Registration of Drugs from 1948 to 1961 and served as Secretary and then President of the Commission of the Italian Pharmacopeia. Shortly before his retirement, he was also still chairing the Special Parliamentary Commission on patents for pharmaceuticals.

Close ties with industry in research projects tainted the Institute's institutional duties of controlling the registration of specialità medicinali, its key role in fixing their prices and in inspecting the drug firms. Archaic legislation on the registration of specialità medicinali and the authorisation of officine farmaceutiche, failed to generate incentives for investment in fundamental and clinical research and hampered its much needed scientific support in the 'modernisation' of the industry and the clinic. This also created insidious fault lines within the Institute. A schism developed between scientists doing fundamental research and technicians assigned to more mundane service activities, such as drug registration and state controls[17]. This conflict between service and research activities is best exemplified by the polar positions of Giuseppe Penso and Mario Ageno, both influential directors of important labs. Ageno stuck to the mission Marotta had defined in 1942: 'the Institute ought to be, basically, an institute for scientific research. The main task of its personnel must be pure research, completely free and disinterested, set free from whatever practical or applicative goal'. For him, pure research was also the best possible training for civil servants in charge of controls and inspections. Conversely, Penso severely criticised Marotta for perverting the Institute's original regulatory mission, and for his policy of progressively removing administrative controls.

The Marotta affair: a drama in three acts

The Marotta affair essentially typified the difficult institutionalisation of the two main features associated with modern postwar scientific research: the teamwork mode of organisation and the close

linkage between research and commercial interests. The drama developed in three acts: the Beecham mishap, the parliamentary debates and Marotta's trial.

The first act of the drama was mostly played out within the scientific community, but also had significant commercial effects which fully manifested later[18]. Since the mid-1950s, Chain had been cultivating strong consultancy ties with the Beecham Group. Negotiations between lawyers were protracted, but in the meantime, while a new fermentation plant the company was building in London with Chain's advice was under construction, a small group of researchers from the company was being accommodated in Rome. The collaboration culminated in the isolation of 6-APA, which paved the way to a number of clinically valuable and very profitable semi-synthetic penicillins. However, if Beecham researchers shared (possibly unfairly) the scientific credit with their Italian hosts, the British company took all commercial profits. Chain later declared that 'I had a tremendous amount of unpleasantness in Rome following the announcement of the 6-APA discovery at Brockham Park, and so had Professor Marotta'. Part of the unpleasantness came from 'a lot of ill-feeling' among his collaborators in Rome who, because of Chain's private arrangements with Beecham, were kept in the dark during the subsequent development of the work they had initiated at the Institute with their English guests. Chain explained that the contract his lawyers had negotiated prohibited him from fully informing his co-workers of further developments of the work they had initiated in Rome and jointly decided 'to follow up at some later convenient time'.

The Beecham mishap demonstrates the problems surrounding the attribution of credit which arise from the teamwork typical of the organisation of postwar 'big science', problems which Chain himself had encountered in his Oxford years[19]. Chain's behaviour was a clear break with the Mertonian values of communalism and disinterestedness, which require full disclosure of scientific findings irrespective

of personal interests. Chain's private contractual relationship with Beecham adds a further category to the three modes of relationships between scientific and commercial interests, as described by Swann and further elaborated by Rasmussen, where conditions of collaboration are spelled out explicitly in legally binding and usually secret private agreements[20].

More 'unpleasantness' was to come in the parliamentary debate about the 'fourteen questions to the minister Jervolino' made by the communist MP, Messinetti, in the Camera dei Deputati on 22 October 1963. Mentioning the Beecham story and referring to the many semi-private institutions that had mushroomed in the shadow of the Institute, Messinetti condemned the institutional and personal conflicts of interest which the internal governance of the institute nurtured. His claim was that 'consultancy to private companies, whose products are controlled by the technicians of the Institute must be absolutely forbidden…. Integration between the controller and the controlled ought to be banned'. The press covered the scandal extensively. *L'Espresso*, a left-leaning weekly, blamed Chain for having 'patented and ceded to an English firm a new technology invented in the Institute and in collaboration with its technicians', and Marotta's long and autocratic ruling of the Institute inspired parallels with 'South-American kings of cocoa'. Other more restrained comments focussed on the poor conditions of the public administration ('administrative lapses and wrongdoings are inescapable facts for the Institute, a state of necessity due to its organisation'), an issue which was later taken by researchers to vindicate their behaviour.

The parliamentary debate was just the beginning of the storm. A few months later, Marotta and his successor Giordano Giacomello, together with the administrative director and the financial officer of the Centers, were all prosecuted on various charges of malfeasance and misappropriation of public funds. The scientific community mobilised, in Italy and abroad, with Chain active participating from

his safe harbour within the Imperial College[21]. Outdated legislation was the culprit and, in the eyes of the Italian scientific community, 'così fan tutti' was the main justification. Chain acknowledged that Marotta's methods were 'not orthodox' but 'he did as all people do in Italy'. As for the motives, according to Chain 'Marotta used these methods only because of the great love he bore for the Institute', and after all, 'not a single penny ended up in his pockets'. One scientist, commenting anonymously in the Parisian newspaper, *Le Figaro*, claimed that 'legislation is behind the times. In matters of administration the laws do not permit the development of research except by methods which do not always seem strictly orthodox'. An anonymous 'scientist-administrator' told the journal *Science* that 'given the archaic character of the administrative laws of the Italian state, all directors of institutes inside and outside the Universities are obliged to act this way. This is well known and tolerated by central authorities'. Bovet's remarks to the *London Times* added a significant twist to the apparently unquestionable fact that 'almost all true researchers in state organisations were guilty of more or less big, though only formal, crimes against the administration'. His additional concern was that the new state of affairs empowered what he called 'the subordinates', in that 'any subordinate now has to hand the instruments he needs to make his superior tremble'. However, what scientists described as a necessary behaviour to curb bottlenecks and administrative red-tape went strongly against the legalistic culture of the judiciary. In the drama, the abstract logic of the law was personified by the prosecutor Ricciardi, who was described as pursuing 'the superiority of the law over arbitrary acts of individuals'. The traditional tension over the mission of the Institute now emerged as a 'deviation', worthy of punishment under the law. The *London Times* captured the spirit of the time, observing that 'the almost whimsical side of the sorry story is that state institutions have the money for research; it is just that they will now be afraid to use it'. In fact, the thunderstorm

hit the Italian scientific community when Italian science was apparently in a much better shape than ever[22]. A large conference held in Rome in 1961 under the chairmanship of Malfatti and Giacomello (who succeeded Marotta as director of ISS and shared his fate in the trial) is regarded as the beginning of serious debate about science policy in Italy. The conference linked scientific research, higher education and social and economic development for the first time and exposed the technology gap between Italy, Europe and the US. An official commitment to support science was included in the program of the centre-left government, which in 1963 increased the budget for science to 0.6 per cent of the gross national product. The arrest of Marotta, along with the traditional vagaries of Italian politics, halted a much needed change in the organisation of Italian science.

The tragedy of the Marotta affair was that apparently no lesson was learnt. The new managerial culture of big science was transforming life scientists from laboratory investigators into administrators of large programs. Ever bigger business was reshaping the boundaries between public knowledge and private profits, initiating an insecure new 'moral economy' where the old Mertonian principles of the scientific community were as inadequate as the archaic administrative regulations of the State. The perception of a technology gap had raised serious doubts over the continuation of the 'economic miracle' of the late 1950s, which had been presciently explained as a short-lived and self-limiting episode of catch-up after a long period of stagnation[23]. The early signs of an impending decline would be principally revealed in the more knowledge-based sectors of the economy, such as the pharmaceutical industry, which had undergone the worldwide revolution that had apparently saved Italy[24]. The Italian pharmaceutical industry adapted well to the postwar climate of radical technological change, fierce competition over new products and diminishing prices, by buying licences from foreign firms, reverse engineering their production processes and overflowing the

drug market with copies of the same substances. Protectionist legislation safeguarded the domestic market, the archaic regulation of which was poorly policed. Low wages and high prices ensured fat profits to an industry which successfully resisted 'Americanization' during the reconstruction years and, later, 'Europeanisation'. A contemporary witness crudely summarised reasons for the backwardness of Italian industry: 'We produce by copying rather than studying because it is much more profitable to re-make than to make, much more convenient to copy than to take risks, and this imitation needs just small brains and little money, small men in small firms'. However, this succeeded for short-term profits rather than long-term prospects and did not prevent the slide into technological and economic dependency on other countries. Acquisition, the most obvious sign of economic and technological dependency, started in the knowledge-based sector of pharmaceuticals and in the production of penicillin particularly, at the cutting edge of the technological frontier. As early as 1947, the American multinational Squibb had bought Palma to sell penicillin and later streptomycin on the Italian market. This was the start of the pharmaceutical industry's slide into technological dependency, and the transformation of Italy into a consumption market for drugs in the late 1950s and 1960s.

Concluding comments

The postwar world of 'big science and bigger business' was not a place for insular institutions in science, or for 'small men and little money' in industry. In the early postwar years, science was essentially conceived by the Italian government as a cultural engagement to be left for better times. Science policy was only given serious consideration in the early 1960s, when its contributions to the social and economic growth of the nation became a political issue. The absence of a policy for science left the sheer survival of scientific enterprises to the initiative of isolated individuals and their personal

connections. Political manoeuvring invited secrecy of means and ambiguity of goals, which contributed to distorted priorities in the allocation of scarce resources and fostered 'the enclosure effect', where each (marginally) successful institution 'perceived itself as a pole of excellence and did not develop any contact with other similar institutional frameworks'[25]. In essence, this explains why the spending of a huge amount of precious money for the fabbrica della penicillina gave so little in return. Transforming the only public health agency of the state into one of many world-renowned research centres actually worked against the modernisation of the pharmaceutical industry and hampered the regulatory capabilities of a public administration maintaining an archaic legislation. The tunnel visions and soaring ambitions of Marotta and Chain, together with the absence of a science policy and the presence of the liberal protectionism which guided the postwar reconstruction process, helped to keep the Italian pharmaceutical industry on its remunerative path of small risk and high profits in a protected market: a strategy for short term profits, not long-term prospects.

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6. See for example EINAUDI M., *Political issues and alignments in Italy today*. Review of Politics 1944; 6(4): 484-515; STANDEN N., *Italian backdrop*. Harper's Magazine 1948; 196: 150-159. On health and health care see also quotations from UNRRA reports in SALVATICI S., *'Not enough food to feed the people'. L'UNRRA in Italia (1944–1945)*. Contemporanea 2011; 14(1): 83-99; BUD R., *see* note 3, p. 85.
7. On science and reconstruction in postwar Italy, see the speeches published in the official journal *Ricerca Scientifica e Ricostruzione* by the CNR president Colonnetti, Prime Minister De Gasperi, and Luigi Einaudi; COLONNETTI G., *Il discorso di S.E. Gustavo Colonnetti*. Ricerca Scientifica e Ricostruzione 1945; 15(1): 4-10; COLONNETTI G., *La ricerca scientifica e la ricostruzione*. Ricerca Scientifica e Ricostruzione 1945; 15(6): 509-511; COLONNETTI G., *Il discorso del Prof. Colonnetti*. Ricerca Scientifica e Ricostruzione 1946; 16(1-2): 5-11; COLONNETTI G., *Discorso dell'On. Prof. Gustavo Colonnetti*. Ricerca Scientifica e Ricostruzione 1947; 17(12): 1916-1927; COLONNETTI G., *Discorso. Assemblea plenaria dei Comitati nazionali e dei Centri di studio*. La Ricerca Scientifica 1948; 18(7): 733-745. By prime minister; DE GASPERI A., *Il discorso dell'On. De Gasperi*. Ricerca Scientifica e Ricostruzione 1946; 16(1-2): 12, and EINAUDI L., *Discorso dell'On. Prof. Luigi Einaudi*. Ricerca Scientifica e Ricostruzione 1947; 17(12): 1932-1933.
8. For different (gu)estimates of the total cost see COZZOLI D., CAPOCCI M., *see* note 1; BOVET D., *see* note 1; GUALANDI G., *Il Centro Internazionale di Chimica Microbiologica ed il suo capo E.B. Chain. Domenico Marotta nel 25° anniversario della morte*. Rendiconti Accademia Nazionale della Scienza detta dei XL. 1999 (211-222). The budget for TB community services is from parliamentary records. For CNR budgets see COLONNETTI G., *Discorso dell'On*, *see* note 7.
9. Quotations are from Chain's notes as reported in CLARK R.W., *see* note 3, p. 115 et passim.
10. Quotation is from BUD R., *see* note 3, p. 88. References to Italian scientific traditions and the right to obtain a seat with the Great Nations occur frequently in Colonnetti's speeches.

11. See personal recollections of Gualandi, one of 'Chain's babies' in Rome who also followed his chief to ICI to help install the new lab; GUALANDIG., *see* note 8. Reports of the ISS collaboration with the WHO are in WORLD HEALTH ORGANIZATION, *Supplementary Report of the Interim Commission to the First World Health Assembly. Stimulation of the production of penicillin*. Official Records no.12. Geneva, WHO, 1948; WORLD HEALTH ORGANIZATION, *Expert Committee on antibiotics. Report of the First Session*. World Health Organization, Technical Report Series no.26. Geneva, WHO, 1950. Chain's profile was published anonymously by *New Scientist* in the wake of the isolation of 6-APA, and the tribute to the ISS and his director appears as a sort of posthumous reparation of the credit (and the profits) accrued by Beecham; NEW SCIENTIST, *Profile. Ernst Boris Chain. A pioneer of penicillin research*. 1959; 19 March 5(122): 636-638. The value of the centre in opening up the market for antibiotics to the Italian industry is claimed in POCCHIARI F., *Lo sviluppo delle biotecnologie in Italia: intuizione e ruolo di Domenico Marotta*. Annali dell'Istituto Superiore di Sanità 1990; 26(1) Suppl: 15-20.
12. The paper was based on the speeches delivered during Marotta's conference trip to Romania in 1942 and was published the following year; MAROTTA D., *Aspetti dell'organizzazione sanitaria italiana*. Rendiconti Istituto Superiore di Sanità 1943; 6: 315-338. The text of the paper is remarkably free of the traditional praise of the fascist regime and its leader, which was *de rigueur*, particularly when visiting a fascist country. This is taken by Cerruti to be an example of Marotta's 'political agility' and proof of his 'quick sensibility' to changes in the political climate; CERRUTI L., *Domenico Marotta. Dai Laboratori di Sanità Pubblica alla fondazione dell'Istituto*. Rendiconti dell'Accademia Nazionale delle Scienze detta dei XL 1999; 23: 91-133.1999). On the negotiations between Missiroli, Hackett and Marotta about the mission of the new Institute and later developments, see CERRUTI L., *idem*; DONELLI G., SERINALDI E., *Dalla lotta alla malaria alla nascita dell'Istituto di Sanità Pubblica*. Bari, Laterza, 2003; STAPLETON D.H., *Internationalism and nationalism: the Rockefeller Foundation, public health and malaria in Italy, 1923–1951*. Parassitologia 2000; 42(1-2): 127-134; COZZOLI D., CAPOCCI M., *see* note 1. The text of the agreement between the ISS and the Rockefeller Foundation signed by the Italian government is in CERRUTI L., *idem*.
13. The concept of the continuity of the state in men (sic!) and institutions from the liberal, pre-fascist state to the republic and through the fascist regime is

originally from PAVONE C., *Sulla continuità dello Stato, 1943–45*. Rivista di Storia Contemporanea 1974; 3(2): 172-205. For an insightful examination of the development of public administration, see MELIS G., *La cultura dello Stato fra continuità e discontinuità*. Quale Stato 2006; 4: 393-405. An empirical analysis in the context of Enti pubblici as the ISS was is in SALVATI M., *Gli Enti pubblici nel contesto dell'Italia fascista*. Le Carte e la Storia 2002; 2: 28-41; SALVATI M., *Behind the cold war: rethinking the left, the state and civil society in Italy (1940s–1970s)*. Journal of Modern Italian Studies 2003; 8: 556-577.

14. Marotta's mentors and models, as mentioned in his acceptance speech at La Sapienza, are in CERRUTI L., *see* note 12. The special interest and support of De Gasperi is claimed in MAROTTA D., *L'Istituto Superiore di Sanità*. Roma, 1963, p. 10.
15. Quotation of Chain's attitudes is from CLARK R.W., *see* note 3) and NEW SCIENTIST, *see* note 11.
16. On Chain's general attitudes toward the pharmaceutical (and later also the food) industry see, for example, the very positive comments he made at the Royal Society Conference in the midst of the thalidomide scandal. The paper based on the conference speech was published in several journals, including *Nature*; CHAIN E.B., *Academic and industrial collaboration to drug research*. Nature 1963; 200: 441-451. Chain's eagerness to enter the commercial field had been widely known since his famous altercations ('violent discussions' as he described them) with Mellanby over the patenting of penicillin. The major domo appellation is from MCGRAW D.J., *On leaving the mine. Historiographic resource exhaustion in antibiotic history*. Dynamis 1991; 11: 415-436, p. 431.
17. See AGENO M., *Riflessioni e proposte per la riforma dello ISS*. Roma, 1963; PENSO G., *L'Istituto Superiore di Sanita' delle sue origini a oggi: esegesi storica e prospettive per il futuro*. Roma, Tipografia regionale, 1964, p. 57 et passim; Plus specific comments in COZZOLI D., CAPOCCI M., *see* note 1.
18. This intricate story is recounted with slight differences in CLARK R.W., *see* note 3, p. 132 et passim and BUD R., *see* note 3, p. 124 et passim. While it is beyond doubt that commercial profits only went to Beecham, whether scientific credit was apportioned fairly is less obvious. Authorship of the first paper published in the 17 January issue of *Nature* was shared by both groups, with the names of the Italian group (Chain included) first; BALLIO A., CHAIN E.B., DENTICE DI ACCADIA F., ROBINSON G.N., BATCHELOR F.R., *Penicillin derivatives of P-amino benzylpenicillin*. Nature 1959; 183:

180-181. The second paper, published one week later on 24 January recognised only the researchers from Beecham; BATCHELOR F.R., DOYLE F.P., NAYLER J.H.C., ROBINSON G.N., *Synthesis of penicillin: 6-aminopenicillanic acid in penicillin fermentation*. Nature 1959; 183: 257-258. However, while the first paper dealt with 'discrepancies...observed between chemical and biological methods of penicillin essay', the second reported 'the isolation of pure 6-amino-penicillin-acid'. This second paper is therefore the only paper that has been cited later as the source of the important discovery of Penbritin, 'the penicillin invented in Britain'.

19. Chain felt he had not received the credit he deserved in Oxford, perceiving Florey's mission to the US as 'a underhand trick and act of bad faith'; CLARK R.W., *op. cit*. note 3, p. 53. The two volumes written by the Oxford team on the history of the discovery of penicillin were, in his opinion, 'a travesty of true facts' (*idem*, p. 114), conjured up by 'the systematic and carefully planned efforts of Fleming' as he wrote to Florey (*idem*, p. 99). About Florey, however, his notes report that 'Florey's behaviour to me in the years 1941 until October 1948, when I left Oxford for Rome, was unpardonably bad' (*idem*, p. 46).
20. The transmission of knowledge from the academy to the industry through individual consulting by academic staff was later institutionalised through legally binding contracts, either personal (such as in Chain's case with Beecham) or, more frequently, between organisations. A further step adopted more sophisticated transfer mechanisms, such as patenting and the selling of licences and commercial spin-offs of the parent organisation.
21. On Chain see SHEPPARD J., *Sir Ernst Boris Chain and the International Centre for Microbiological Chemistry at the Istituto Superiore di Sanità*. Rendiconti dell'Accademia Nazionale delle Scienze detta dei XL 1999; 23: 197-209.; CLARK R. W., *see* note 3. On the international media campaign, see MCELHENY V.K., *Research climate in Italy*. Science 1964; 145: 690-693; MCELHENY V.K., *Research climate in Italy II*. Science 1965; 148: 205-207.
22. The 1961 Conference organised by the Christian Democracy was a major event, participated in by Italian scientists working in Italy and abroad. The proceedings enjoyed a wide audience; GIACOMELLO G., MALFATTI F.M. (eds), *Una politica per la ricerca scientifica*. Roma, Edizioni 5 Lune, 1962. Abstracts were also published as a special section of the international journal *Minerva*; MINERVA, *The reform of the organization of scientific research in Italy*. 1964; 2(2): 225-231.1964; GIACOMELLO G., MALFATTI F.M.,

Scientific research, economic development and higher education. Minerva 1964; 2(2): 210-224.

23. See, in particular, the insightful and prescient analysis of the Italian economic miracle by Beniamino Andreatta; ANDREATTA N., *Fattori strategici nello sviluppo tecnico della industria italiana, 1938–1958*. In: *AA.VV. Il progresso tecnologico e la società italiana. Vol I. Effetti economici del progresso tecnologico sull'economia industriale italiana, 1938–1958*. Milano, Giuffrè, 1962, pp. 13-27.
24. For a general history of the pharmaceutical industry in Italy, see SIRONI V.A., *Le officine della salute. Storia del farmaco e della sua industria in Italia*. Bari, Laterza, 1992. Reports from contemporary witnesses on the status of the drug industry in the 1940s and 1950s include CARRARA G., *L'industria farmaceutica italiana nel 1947 di fronte all'industria farmaceutica nel mondo*. La Chimica e l'Industria 1947; 29(8-9): 208-210; CARRARA G., *Realizzazione e prospettive dell'industria farmaceutica italiana*. Il Farmaco 1950; 5(5): 571-575; SOLDI A., *L'industria farmaceutica italiana dopo la guerra e le sue prospettive future*. Il Farmaco 1951; 6(6): 614-624; SOLDI A., *Situazioni e prospettive dell'industria farmaceutica nazionale*. Il Farmaco 1953; 8(4):165-176; SOLDI A., *La situazione odierna dell'industria farmaceutica in Italia*. Il Farmaco 1958; 13(11): 569-580. The quotation is from SOLDI A., *Situazioni*, *idem*.
25. GEMELLI G., *The 'enclosure' effect: innovation without standardization in Italian postwar education*. In: ENGWALL L., ZAMAGNI V., (eds) *Management education in an historical perspective*. Manchester, Manchester University Press, 1998, pp. 127-144; GEMELLI G., *Epsilon effects. Biomedical research in Italy between institutional backwardness and islands of innovation (1920s–1960s)*. In: GEMELLI G., PICARD J.F., SCHNEIDER W.H. (eds), *Managing medical research in Europe. The role of the Rockefeller Foundation (1920s–1950s)* Bologna, CLUEB, 1999, pp. 175-197. The 'enclosure effect' (GEMELLI G., *The 'enclosure' effect*, p. 117) has originally been described as the behaviour of Italian schools of management under the modernisation push of international (mostly US-led) initiatives of the early 1950s. In Gemelli's description, each school perceived itself as a self-sufficient and autonomous centre of excellence and did not strive for exchanges with similar or complementary organisations. Each island of (self-perceived) excellence tended to create its own archipelago, which eventually transformed into an enclosure 'bound for mere survival'. Analysing the failure of other modernising ventures in the biomedical field, Gemelli has

pointed out that 'they became islands of innovation without achieving much cross-fertilisation, especially with the university system' (GEMELLI G., *Epsilon effects*, p. 194). Her analysis echoes the excoriating comments on the 'fiefdoms' of the 'feudal structure' of Italian universities in the 1950s made in the report to the US National Science Foundation published in *Science* in 1961; CONSOLAZIO W.V., *Dilemma of academic biology in Europe*. Science 1961; 133: 1892-1895.

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