The Novartis Agreement: An Appraisal

Administrative Review, October 4, 2002

Robert M. Price, Associate Vice Chancellor for Research
Laurie Goldman, Director of Planning and Analysis, VCRO

EXECUTIVE SUMMARY

The Novartis Agreement was initiated in a veritable storm of controversy. Commentators from within and without the University raised the specter of significant adverse institutional consequences for the Department of Plant and Molecular Biology as well as for the Berkeley campus generally. This review has found that in practice the Novartis agreement has been quite different than what these critical commentaries expected. Indeed, virtually none of the anticipated adverse institutional consequences has been in evidence. The Novartis Corporation and its successor, Syngenta, have assumed a "hands-off" posture with respect to the research conducted by PMB faculty, post-doctoral fellows, and graduate students. The industry representatives on the Novartis program's Advisory and Research committees have not attempted to steer PMB research in any particular direction. They have been willing to support the research projects proposed by departmental faculty, in the same manner as the departmental and campus representatives on these committees. We are aware of no instance in which the industrial "collaborator" sought to target its funding to particular research questions, or in any other way attempted to influence the research direction of PMB laboratories. Nor has the Novartis Corporation, or its successor, blocked the publication of research results emanating from PMB laboratories.

There has been no noticeable movement in PMB's research agenda toward "applied research," as was widely anticipated. Rather, there is a marked continuity with respect to the basic subjects of PMB's scientific inquiries, while a movement to incorporate the latest advances in genomics and bioinformatics into those inquiries has been facilitated by the Agreement. According to the PMB faculty, the availability of five years of almost certain Novartis funding has allowed them to pursue more novel and innovative lines of inquiry then would have been possible had they had to rely on the usual sources of extramural research funding. At the same time, PMB faculty members have continued to supplement their Novartis funds with extramural research support from other sources. The Novartis program constitutes a significantly smaller proportion of PMB's total research funding today than was the case at the outset of the collaborative relationship (approximately 27% in 2001-2002 compared to 73% in 1997-1998).

The Agreement's stipulation that all PMB participating researchers present abstracts of their papers to Novartis thirty days prior to submission for publication has been honored, but researches do not think that the practice has had any significant impact on the date of actual publication. PMB faculty members have increased somewhat the pace of their publishing since the Agreement's initiation, but the large number of patent filings by Novartis, which some anticipated, has not materialized.

The Novartis Agreement has had a significant impact on graduate student recruitment. With the funds it made available for graduate fellowships, PMB has been able to stay competitive with respect to recruiting the very best graduate student

prospects. This fellowship money has been used to support first and second year graduate students. It is not targeted to students with any particular research interest, as some anticipated it might be. Beyond the effect on resources available for graduate student support, the Agreement has not significantly altered the nature of graduate or undergraduate education within PMB. Faculty members teach the same number of courses as before the Agreement's inception, and the curriculum has remained in tact, with the notable addition of several courses in genomics and in microbial biology. The involvement of scientists from Novartis in the supervision of graduate students, anticipated by some, did not materialize.

Given the positive benefits that have accrued to PMB, it is no surprise that the department faculty would wish to continue the existing arrangement into the future. Whether the Agreement is renewed or not is a matter that lies with Syngenta and thus is beyond the scope of this review

COLLABORATIVE RESEARCH AGREEMENT, No: 010134
"THE NOVARTIS AGREEMENT"

INTRODUCTION

In the winter of 1998, the University of California entered into an agreement with the Novartis Agriculture Discovery Institute (NADII) that provided twenty- five million dollars of research support, $5 million per year for five years, to Berkeley's Department of Plant and Microbial Biology (PMB). Controversy erupted as knowledge of the impending agreement spread to the campus community and beyond. Various committees of the Academic Senate, as well as individual members of the Berkeley faculty, the mass media, and the California State Legislature, expressed concerns about what they considered possible, even likely, adverse consequences of the "Novartis Agreement." Although the Dean of the College of Natural Resources, who was a central figure in negotiating the agreement, sought to allay these concerns with extensive oral and written testimony, the concerns persisted. Thus, in a letter to Executive Vice Chancellor Christ, the Chair of the Academic Senate expressed the Senate's continuing reservations, set forth the view that the agreement would have "varied and broad institutional impacts," and called for the establishment of safeguards "to avoid the adverse institutional impacts of the sort that are now being discussed on campus, in the press and … by Students for Responsible Research."[1] One week later, the Senate leadership expressed its concern "regarding the potential for an unhealthy narrowing of the nature and direction of the Department's [PMB's] research agenda . . . to issues principally of interest to Novartis."[2]

> *"[Novartis will be] an 'elephant' in the department—an elephant, moreover, whose motives are not those of the University. Such an enterprise cannot be fairly compared with . . . funding by a disinterested foundation or government agency, in which the donor in effect 'backs off' after making the contribution. This donor will remain among us, trying to influence department research policies*." [Member, Committee on Academic Freedom, quoted in DIVCO questions to EVC Christ]

For most of the Novartis Agreement's critics, like the one quoted above, it was the corporate-industrial source of research funding, and the fact this stream of industry research funds was to be concentrated in a single department, that raised concerns about potentially adverse institutional consequences. Critics reasoned that as a profit-driven enterprise, the "private" interests of the Novartis Corporation (or its successor, Syngenta) are not and could not be the same as the "public" interest of the University, i.e., to create and to freely disseminate knowledge. This "contradiction of interests," it was feared, would divert the University from its appropriate mission, as its private partner, Novartis, sought returns to the capital it was investing in PMB's research. For some, this line of reasoning produced particularly intense opposition to the agreement, since they opposed

[1] Letter from Robert Brentano, Academic Senate Chair, to EVC and Provost Carol Christ, November 18, 1998, p. 2 and 3.

[2] Professor Robert Spear, "Academic Senate Comments on Novartis Agreement," November 23, 1998, p. 1.

the development of genetically modified food, which they assumed it was Novartis's agenda to promote.

The specific concerns that emerged from the debate surrounding the signing of the Novartis Agreement can be grouped into four broad categories:

- concerns about the Agreement's impact on the governance of PMB
- concerns about the Agreement's impact on the amount, direction, and type of research conducted by PMB faculty, graduate students, and postdoctoral fellows
- concerns about the Agreement's impact on the free flow of university created scientific knowledge, as well as on the atmosphere of open intellectual exchange among members of the university community
- concerns about the Agreement's impact on graduate and undergraduate instruction

It was in response to the controversy generated by the Novartis Agreement and to the expression of concern from the Academic Senate that the idea of this administrative review emerged. Other examinations initiated by the campus have also been undertaken, and a large study by an external research group is currently under way. We have structured our review so as to give primary attention to the concerns raised about the potentially adverse operational/institutional consequences of the PMB-Novartis relationship, treating these concerns as hypotheses to be tested. What exactly, we want to know, has occurred in PMB since the inception of the Novartis Agreement? Have the department's operations and performance changed, and if so, in what manner? If changes have occurred, are they the adverse ones anticipated by the Agreement's critics? To answer these questions we have, whenever relevant and possible, utilized data available from campus sources. This "hard data" has been supplemented by interviews with eighteen faculty members, five graduate students, two postdoctoral fellows, and the member of the PMB administrative staff with responsibility for the Novartis Agreement. We also conducted a telephone interview with the CEO of the Torrey Mesa Research Institute (TMRI).

BACKGROUND

In 1989, the campus established the Department of Plant Biology, within which a new graduate curriculum was developed in contemporary plant biology, with special emphasis on plant development, molecular genetics, physiology, and biochemistry. A Division of Microbial Biology was added in 1996 and the department's name was changed to the current Department of Plant and Microbial Biology (PMB). Currently, the department has a complement of twenty-seven regular faculty members, five of whom are members of the National Academy of Sciences. In addition, five adjunct professors teach in PMB. At any one time, the department has approximately seventy graduate students as well as one hundred postdoctoral fellows, and some thirty professional staff.

In the mid-1990s, PMB began to actively seek industry funding to support its teaching and research mission. In 1997, in an effort to maximize financial support and

technological benefits, PMB adopted a strategy of seeking a single industrial partner for a research alliance. A "request for proposals" was sent to nine companies, of which six responded. The proposal from Novartis Corporation was selected as most closely matching the PMB conception of a good industrial alliance model. A period of intense negotiations followed. At the request of Novartis, which did not want the terms of its offer made available to the other five companies which had responded to the RFP, the negotiating process was kept confidential. Information about the emerging agreement was tightly held among the campus participants in the negotiations— the Dean of CNR, the VC for Research, the Office of Technology Licensing, and the PMB faculty negotiating team. As a result, few on campus were made aware of the terms or nature of the agreement, except through rumors, until it was at the point of being finalized. This probably explains a good deal of the apprehension and misinformation with which it was greeted once it was made public in late 1998. On November 23, 1998, after eight months of negotiations, a "Collaborative Research Agreement" was signed between the University and the Novartis Agricultural Discovery Institute, Inc. (NADII).

Two years after entering into the Collaborative Agreement, Novartis and another corporation, Astra Zeneca, combined their agricultural divisions to create a new company called Syngenta. It, in turn, purchased NADII from the Novartis Foundation and renamed it the Syngenta Agricultural Discovery Institute (SADII). Shortly thereafter, SADII's name was changed to the Torrey Mesa Research Institute (TMRI). Thus, from early 2001, PMB's partner in the Collaborative Agreement was the successor company, Syngenta, and its agricultural research arm, TMRI. Hereafter, in this report, in order to avoid confusion we will adopt what has become colloquial usage and refer to the PMB-industry partnership as the "Novartis Agreement," or simply as "the Agreement." However, from time to time, when context makes it more appropriate, we will refer to Syngenta or TMRI.

The Agreement

The major provisions of the Novartis Agreement are as follows:

Scope

- The Agreement establishes a 5-year collaborative research relationship between the Novartis Agricultural Discovery Institute, Inc. (NADII) based in La Jolla, California, and UCB's Department of Plant and Microbial Biology.
- NADII provides $25 million in funding over 5 years (2/3 for research, 1/3 for overhead costs) to support basic research in Agricultural Genomics.

Governance

- Oversight of the Research Program is vested in an Advisory Committee, responsible for managing the relationship between the University and NADII, and a Research Committee, responsible for the administration of the PMBD-NADII Research Program funds. The University has a majority of members on both committees.

Research Program

- Research program funds are accessible on a competitive basis to all faculty members in PMB who wish to participate in the collaborative research program.
- Research projects are to be developed by PMB faculty members in areas of their interests.
- Novartis will finance the construction and operation of a research facility "close to the campus of the University."[3]
- PMB faculty, as well as graduate students and postdoctoral fellows, who choose to participate in the Agreement, and who agree to the conditions mentioned below, will have access to Novartis's proprietary genomic bioinformation database, technologies, and scientific equipment.

Intellectual Property

- UCB researchers seeking access to Novartis's proprietary genomic bioinformatics database and microarray technology must sign an agreement not to disclose, without the permission of Novartis, the proprietary information so obtained. The non-disclosure agreement is binding for the duration of the Collaborative Agreement, plus five years.
- Novartis receives the first right to negotiate licenses for a percentage of patentable inventions made in PMB laboratories, based on a ratio of Novartis funding to the total of extramural funds generated by PMB research programs. This formula has given Novartis the right to an option or license on approximately 30 percent of PMB's invention disclosures.
- PMB researchers who choose to sign-on to the Agreement, and the graduate students and postdoctoral fellows in their laboratories, must submit all reports of their research results (publications, papers, abstracts, conference presentations, etc.) to Novartis at least 30 days prior to their release. In the event that Novartis believes patentable subject matter may be disclosed in such reports, and so notifies the University, publication can be withheld for a maximum of an additional 90 days to allow for patent filing by the University's Office of Technology Licensing.

[3] Collaborative Research Agreement, p. 2.

FINDINGS

DEPARTMENTAL GOVERNANCE AND RESOURCE ALLOCATIONS

A commonly articulated perception with respect to the Novartis Agreement is that for the price of $25 million dollars the Novartis Corporation bought itself an academic department. A widely circulated article and "cover story" in the March 2000 issue of The Atlantic Monthly, in which Berkeley and the Novartis agreement were prominently featured, succinctly captured and promoted this perception in its title, "The Kept University." An editorial in Nature (11 January 2001) used the Novartis agreement as an example of the "downside" of industry-university relationships, stating that as a result of its funding commitment Novartis "gains a seat in university and departmental research committees and restricts academics' freedom to discuss the benefits of the deal." The Academic Senate's Divisional Council (DIVCO) described the Novartis agreement as supplying "50% more" than PMB "obtains from multiple outside funding sources," and predicted that, as a result, the PMB environment would be "overwhelmingly dominated by the project and its participants."[4] Among the specific concerns raised by the Academic Senate, in the realm of governance and resource allocations were:

- The role of Novartis representatives in departmental governance and resource allocations-- a role that DIVCO referred to as "major."[5]
- The anticipated appointment of Novartis personnel as adjunct professors-- what role would they play in the Department, in graduate education, in utilization of scarce campus laboratory space? DIVCO anticipated "an expansion of 100 people associated with the private research partner [Novartis]."[6]
- The possibility (for some, the likelihood) that decisions on the allocation of space between PMB and other campus units would be driven by an external funder rather than by academic considerations and decision-making processes.[7]
- The possibility that the Novartis agreement would drive faculty recruitment, department size, faculty salaries, and teaching workloads, producing inequality ("haves/have-nots") among the faculty.[8]

The 'Elephant': Its Size and Shape

Figure 1 presents information on PMB's extra-mural funding sources during the first four years of the Novartis Agreement. It shows the size of Novartis funding, relative to total extramural research funding, as well as the changes in overall funding and fund sources that accompanied the implementation of the Novartis Agreement. During the four year period following the initiation of the Agreement, Novartis/Syngenta was the largest

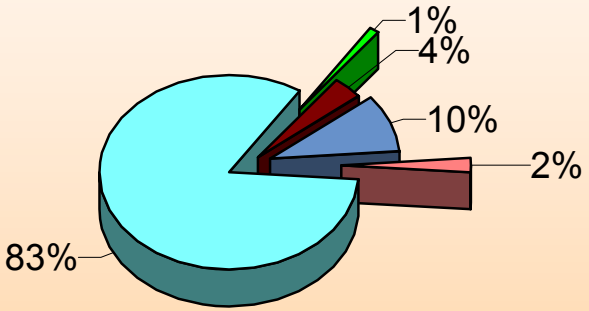
[4] See DIVCO QUESTIONS, "Part IV. Governance of Institutional Evolution, Request for Comment," p. 12.
[5] Ibid., Question 28, p. 13.
[6] Ibid., "Generic Concern," p. 10
[7] Ibid., Questions 25, 26, 26.1, 26.2, 26.3., pp. 10-11.
[8] Ibid., Questions 15, 15.3, 17.2, 19, 20, pp. 8-9.

Figure 1

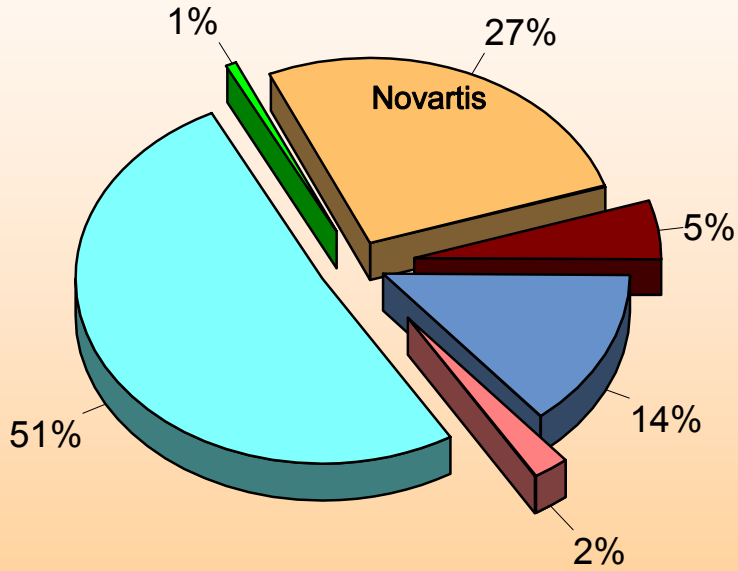
PMB: Funding by Source

Pre-Novartis ('94/95-'97/98)/Post-Novartis ('98/99-'01/02)

Pre-Novartis



Post-Novartis



Total= $27,338,757

Total= $73,882,197

Percent Change = 170%

UC | Non-Profit | Industry | Novartis | other gov't | Federal

Data source: Sponsored Projects Office

single private contributor of research funds to the Department of Plant and Microbial Biology. However, the company's share of the overall extra-mural funding for PMB was considerably less than generally perceived in the media. It was also far less than was projected by those in the Academic Senate who characterized Novartis as an "elephant" based on a projection that its contribution was "50% more" than PMB's entire outside funding. In part, this discrepancy is a consequence of the increase in funding from other external sources received by PMB in the years following the Novartis Agreement's initiation.

At the time the Novartis Agreement came into effect, the PMB faculty was generating approximately $7 million annually in extra-mural research funding (based on a four year running average, AY 1994-95 through1997-98). Hence, if Novartis's $5 million dollars annually was added to this base it would account for 42% of PMB's extramural funds. However, in the four years following the initiation of the Novartis Agreement in November of 1998, PMB's extramural funding increased substantially—from approximately $27.3 million in the four years preceding the Agreement to slightly less than $74 million in the four years after the Agreement's initiation, an increase of $46.5 million or 170 percent. If the $20 million in Novartis money is excluded, the increase in extramural funding was approximately $26.5 million, or 95 percent greater than the total for 1994-1997. **As a result, during the four years subsequent to the start of the Agreement, the Novartis/Syngenta $20 million contribution constituted 27 percent of PMB's total extramural funding.**

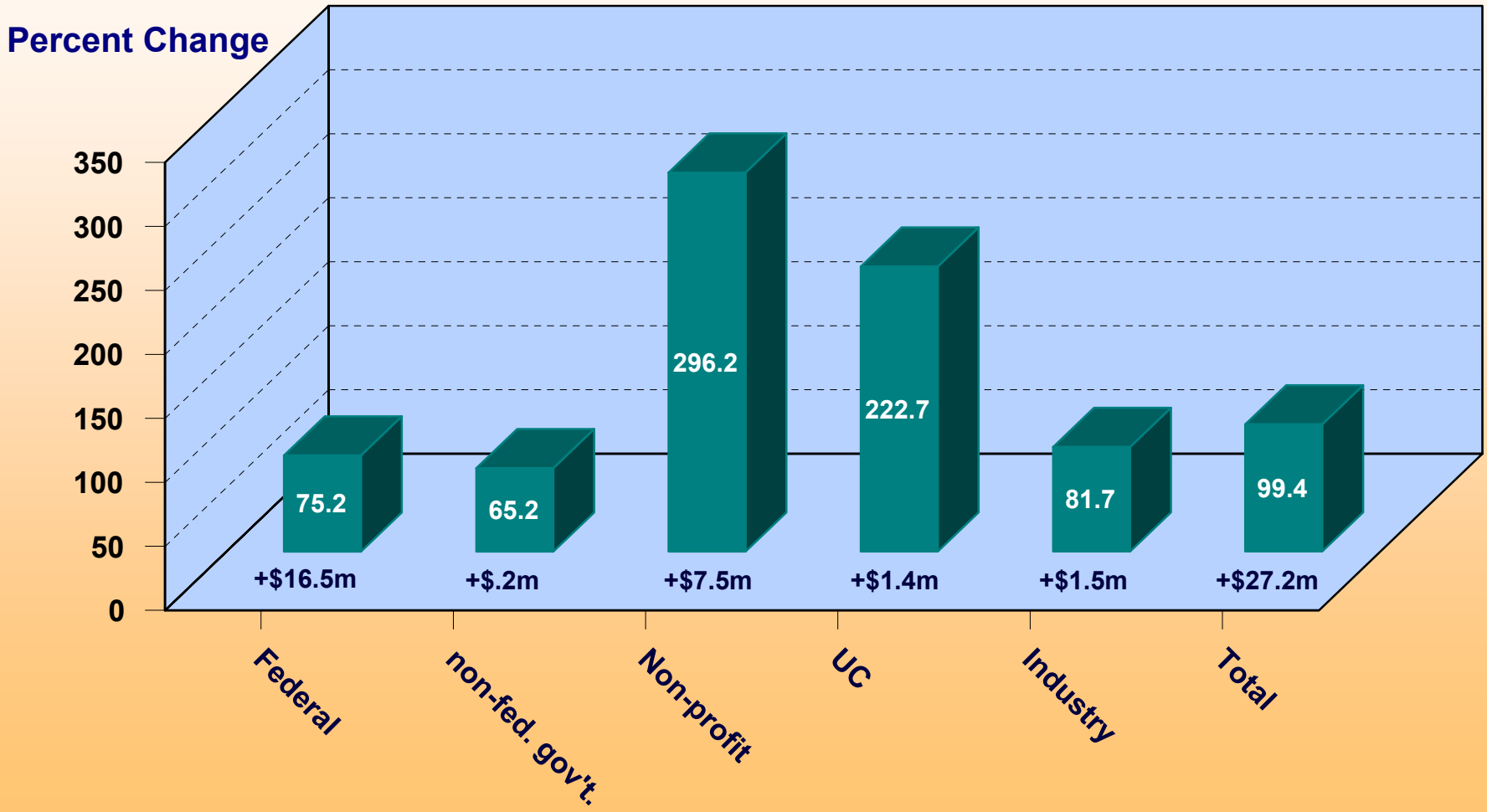
Figure 1 also shows how the relative distribution of funds from among PMB's external funding sources was altered once the campus entered into the Novartis Agreement. The most notable change was in the proportion of research funding obtained from the federal government. In the four years prior to the signing of the Agreement, various agencies of the federal government provided 83 percent of PMB's extramural research funding. In the following four years, while federal agencies continued to be the biggest source of PMB's extramural support, the federal share of the total had declined to 51 percent.

Although declining as a proportion of total research dollars, Figure 2 shows that the absolute amount of federal grant support flowing to PMB increased by $16.5 million in the four years after the Novartis Agreement came into effect, an increase in federal agency funding of some 75.2 percent. Figure 2 also reveals that an increase in extramural funding was recorded, at varying levels, in all funding source categories. The non-profit sector led the way, increasing its funding of PMB research by 296 percent, followed by UC grants (+223 percent), industry, excluding Novartis (+82 percent), federal government agencies (+75 percent) and non-federal government agencies (+65 percent). In the first four years of the Novartis Agreement, 1998 to 2002, industry sources represented 32 percent of PMB's total research support. Companies other than Novartis/Syngenta contributed 16 percent or $3.6 million to this total. (See Figure 3).

Figure 2

PMB: Percent Increases in Funding, by Source

1994-1997 compared to 1998-2002, **with Novartis funding excluded**

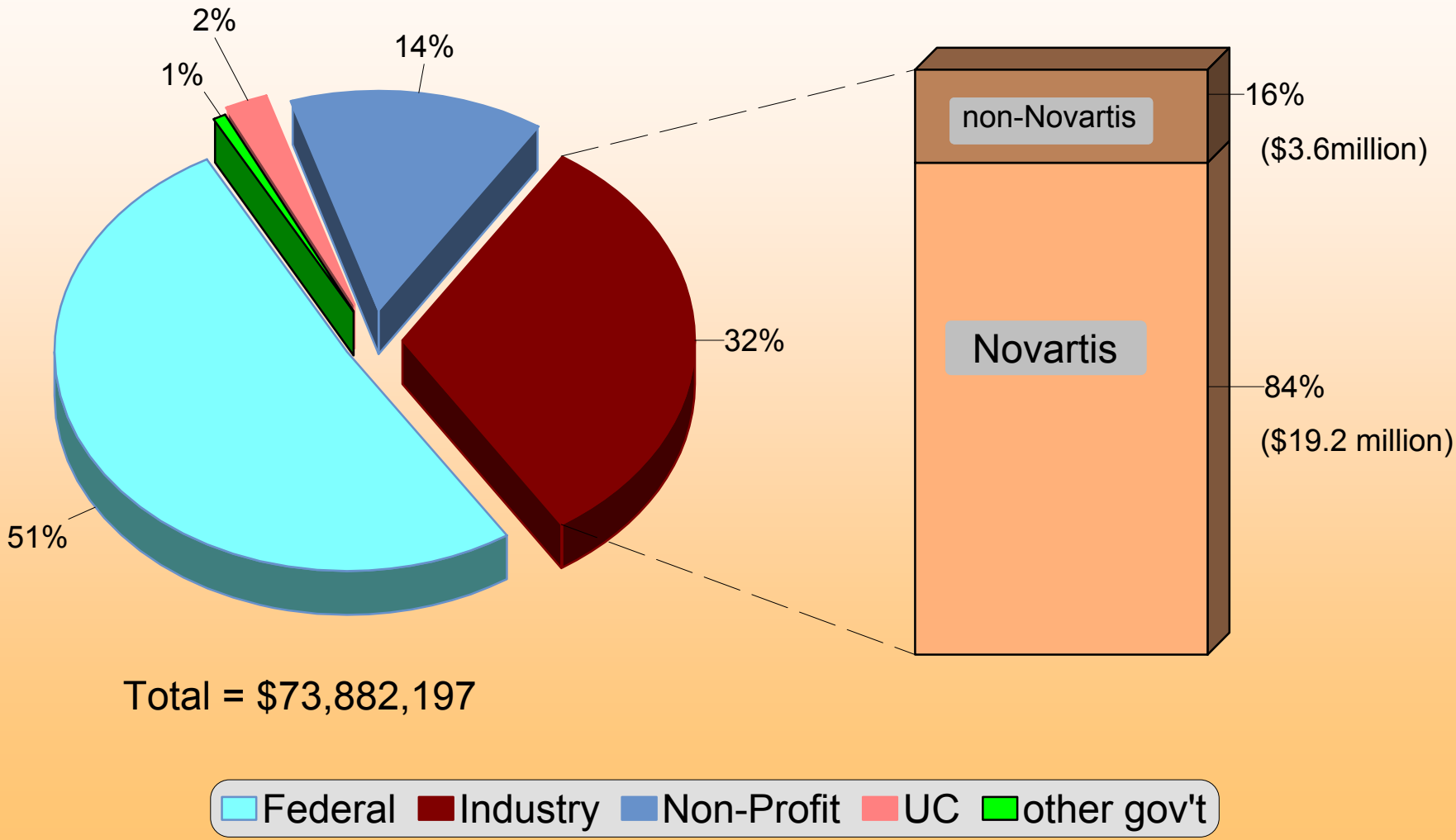


Data Source: Sponsored Projects Office

Figure 3

PMB: Funding by Source

Post-Novartis (1998-2002)



Date Source: Sponsored Projects Office

Governance

Most commentaries on the Novartis Agreement raise the issue of the proper role of external representatives in the governance of academic departments, especially when the external representatives are drawn from industry. Many commentators describe the agreement as granting a significant role to Novartis representatives in the governance of the Department of Plant and Microbial Biology, and even the campus. For example, the Academic Freedom Committee described the Novartis role in PMB governance this way: "[Novartis] employees play such a large role in department policy planning, selection of research priorities, and generally dominate the department by their funding and their active presence . . ."[9] Joined by two other committees of the Academic Senate [COR and ExCom] it asked: "What is the justification for Novartis representatives playing a major role in departmental governance or resource allocation?"[10]

At the outset, it should be noted that with respect to Novartis's role in campus and departmental governance, the Agreement has been widely misperceived and mischaracterized. It did not grant to Novartis representatives any direct role whatsoever in the structures responsible for the general governance of PMB, nor have they played such a role during the period that the Agreement has been in effect. Novartis's "governance role" has been limited to matters related to the research program funded by the company's $25 million grant to PMB, and it has been exercised through minority representation on two bodies, the Research Committee and the Advisory Committee.

Research Committee

The Research Committee allocates up to $3,335,000 per year of the Novartis Agreement funding to research projects proposed by PMB faculty. It has five members—three are members of the PMB faculty and two are representatives of Novartis/Syngenta. Of the faculty members serving on the Research Committee, one is the Agreement's PI and the other two are selected by a vote of the PMB faculty. The Committee is chaired by the faculty Principle Investigator. Currently, the Syngenta representatives are Steven Briggs, the President and CEO of TMRI, and John Salmeron, the Director of the Cereal Gene Analysis Team at Syngenta Biotechnology, Inc. Both of the Syngenta representatives are accomplished research scientists. Briggs works in the area of plant pathology and genetics. He is widely recognized as a leader in corn genomics, and, among other things, is credited with being the first scientist to isolate a disease-resistance gene from plants. Salmeron received his doctorate from Duke University in Botany/Genetics, and was a Post-Doctoral Scholar at UCB from 1989 to 1994.

[9] DIVCO QUESTIONS, p. 14.

[10] "Categories of Interest," Memorandum to the Executive Vice Chancellor from the Academic Senate Ad Hoc Committee on the CNR/Novartis proposal, October 6, 1998, p. 6, question 28.

Current (2001-2002) Research Committee Membership:

Professor Brian Staskawicz, Principal Investigator and Chair (PMB)
Professor Pat Zambryski (PMB)
Professor John Taylor (PMB)
Steven Briggs (Torrey Mesa Research Institute (TMRI))
John Salmeron (Syngenta)

The Research Committee meets once a year to make awards to those PMB faculty who elect to participate in the Agreement. Faculty members submit 2-3 page proposals and awards are made based on three criteria established in Appendix B of the Agreement:[11]

- Quality and intellectual merit of the proposed research
- Potential advancement of discovery
- Past and present productivity of the Principal Investigator

Appendix B also stipulates that **"the Research Committee will not make recommendations to PMBD faculty as to the scope and long-term goals of their proposed research projects."**[12] Interviews with PMB faculty indicate that the Research Committee has operated in the manner set forth in the Agreement. The funding allocations made by the Research Committee will be discussed later in this report.

In the deliberations of Academic Senate committees prior to the Agreement, there was considerable concern expressed about so-called "targeted research"—i.e., research projects that would be mandated or requested by Novartis. We searched for evidence of such targeted research in the descriptions of projects funded by the Research Committee, in our interviews with faculty members and graduate students, and with faculty representatives on the Review Committee. As will be discussed at length later in this report, we found no evidence that targeted research has been part of the Novartis Agreement's implementation. The Novartis Corporation or its representatives do not appear to have sought to give direction to participating faculty or to the Research Committee with respect to either the general direction of PMB research or the foci of specific research projects.

During the four year period under review, each of the participating faculty members (23 out of the 27 regular faculty members in PMB) received some Novartis funding from the Review Committee. The annual awards have ranged from a low of $75,000 to a high of $200,000, with the median of the 23 awards being $125,000. Since faculty participants are likely to receive funding from the Research Committee for all five years of the Agreement, the median funding received by each of their laboratories, over the course of

[11] In the year 3 funding cycle the criteria were modified slightly: 1)originality and creativity of the Proposed Research; 2) conception and organization of the proposed research; 3)broader impact of proposed activity; 4)research progress to date; 5) publications resulting from NADII-supported work. (after the first year).
[12] Collaborative Research Agreement, Appendix B, item 4, para. b., p. 30. [emphasis added]

the Agreement, is something in the order of $625,000. Of the faculty laboratories receiving Novartis funds, approximately half conduct research on genetically modified organisms (GMO's) and half do not.

Advisory Committee

The Advisory Committee consists of six voting members: three representatives from the University (by the terms of the Agreement these are the Vice Chancellor for Research, the Dean of the College of Natural Resources, and a Berkeley faculty member from outside PMB and CNR); and three representatives from the industrial partner. The latter are the President and CEO of TMRI (formerly NADII), and two representatives from the Syngenta Biological Institute (formerly NABRI)). In addition, there are two non-voting members: the current Chair of the Research Committee and the Chair of the Department of Plant and Microbial Biology.

Current (2001-2002) Advisory Committee Membership:

Beth Burnside, Vice Chancellor for Research and Professor, Molecular and Cell Biology
Richard Malkin, Dean of the College of Natural Resources
Jasper Rine, Professor of Molecular and Cell Biology
Steven Briggs, President and CEO of TMRI
John Salmeron, Group leader at Syngenta
Dorothy Pierce, Director of Licensing at TMRI
Brian Staskawicz, ex-officio, Professor, PMB, and Novartis Agreement PI
Andy Jackson, ex-officio, Professor and Department Chair, PMB

The Agreement charges the Advisory Committee with "management of the relationship between the University and NADII during the performance of the Research Program." It also states that the Committee "shall not be responsible for management of the Research Committee or selection of individual research projects . . ." Since the research projects funded by the Research Committee are the essence of the collaborative research program, the Agreement document itself defines a rather limited role for the Advisory Committee. A review of the minutes of the Committee indicates that that has been the case in practice. The Committee has met in Berkeley once each year, with the Novartis/Sygenta representatives "attending" via speaker phone. It receives a general overview of the previous year's research progress, discusses very general issues, and makes minor technical and legal adjustments in the terms of the Agreement. Thus, at its third meeting, on December 17, 2001, the Research Committee's slightly modified criteria for the making of research awards was approved; minor word changes in the Materials Transfer Agreement were adopted; a change of name in the Master Agreement from NADII to TMRI was approved; and suggestions for improved communication between the technology licensing offices of the campus and Syngenta were made. Mechanisms for enhancing the collaborative relationship were discussed and Syngenta representatives suggested holding the annual research retreat in San Diego so more TMRI scientists could participate (the suggestion has been adopted for the October 2002 retreat). Finally,

the Syngenta representatives expressed satisfaction with the way the Agreement was proceeding, and expressed the anticipation that the pace of patent applications would quicken in the later years of the Agreement. Clearly, the Advisory Committee does not play any significant part in the governance of the Department of Plant and Microbial Biology.

Resource Allocations

In addition to the matter of involvement in governance structures, the Novartis Agreement raised a host of questions about the Agreement's impact on the allocation of campus resources. Would the anticipated sizeable Novartis presence on campus, it was asked, distort resource allocations in the areas of faculty recruitment, teaching workload, graduate student support, and space allocations? In answering these and other related questions it will be useful to review how funding generated by the Novartis Agreement, other than that allocated by the Research Committee, has been utilized. Each year the University of California receives approximately $1.7 million dollars in "overhead" from the Novartis Agreement. Half of that amount is retained by the Office of the President and half flows to the campus. Of the approximately $850,000 flowing to the campus, roughly $500,000 per year has been devoted to first and second year graduate student fellowships in PMB. This fellowship support has been divided equally between the Plant and Microbial divisions of the Department. PMB additionally receives approximately $166,000 to support the administration of its two divisions. The remainder of the campus's overhead return goes to the College of Natural Resources, and has been used for things like faculty start-up packages and facilities renovation. In addition, during the initial four years of the Agreement, the Research Committee approved the purchase of some $750,000 worth of scientific equipment. Listed below are the items of scientific equipment purchased with Novartis funds. The listed equipment is available for use campus-wide.

Zeiss 510 UV/Vis confocal microscope*…….	$300k
Zeiss fluorescence stereo microscope …….	$ 75k
High resolution imaging equipment ……	$102k
Deconvolution microscope** ……..	$ 60K
Phosphorimager……	$ 90K
X-ray processor ……	$ 5K
ABI 3100 Sequencer…….	$ 96K
Computers for bioinformatics….....	$ 15K
TOTAL…….	$743K

*MCB, IB and CNR jointly contributed an additional $95K to purchase this instrument.
**NIH provided the core of $265K for this purchase.

The impact of the Novartis Agreement on scarce campus office and laboratory space was another focus of concern by the Academic Senate, which anticipated that a significant

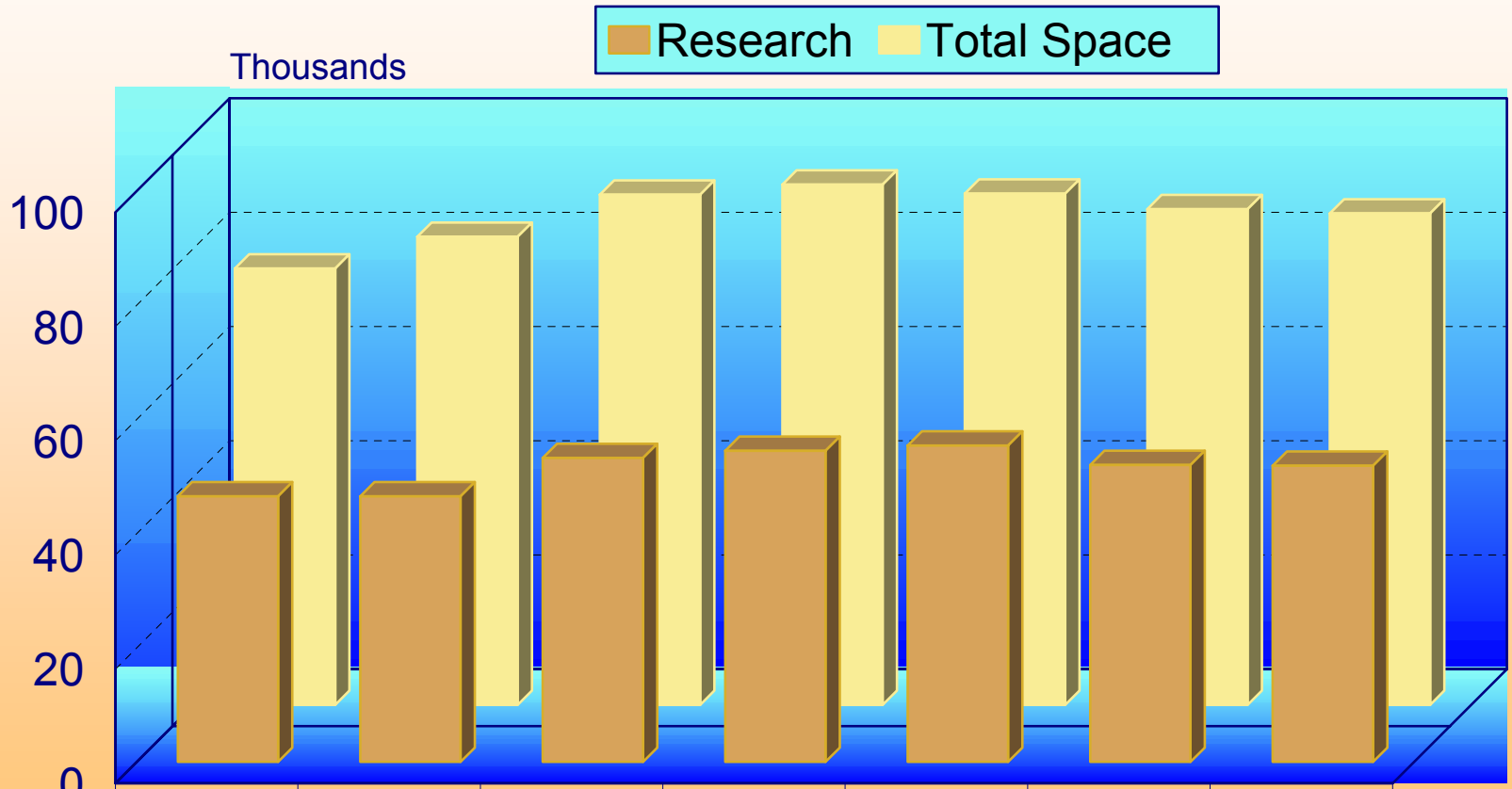
number of Novartis personnel would be working on the campus with their PMB collaborators. This anticipation stemmed from mention in the Agreement of Novartis's intention to establish a research facility close to the University campus. It was further fueled by Novartis's commitment, in early 1999, to provide $5 million for the construction/renovation of a "Research Interface" and $3 million to cover its annual operating expenses.[13] Throughout 1999, discussions took place among various campus stakeholders with respect to where the PMB-NADII research facility might be located—on the campus, on the Oxford Tract, at the Richmond Field Station, in the City of Berkeley. Ultimately, however, the plans for such a facility never came to fruition. Therefore, Syngenta scientists continued to work at the TMRI facility in San Diego, collaborations took place at a distance, and the anticipated involvement of industry scientists in campus life never materialized.

At the time the Agreement was initiated, some in the Academic Senate voiced concerns that the allocation of campus space and of faculty teaching positions would be driven by Novartis funding, rather than by academic criteria. The experience since 1998 reveals that the Agreement has actually had little impact on allocations in these two areas. Since the Fall of 1998, PMB has had two faculty separations and three successful recruitments. An offer to fill another faculty position is currently outstanding. Hence, PMB has experienced, during the period of the Agreement, a net increase of two faculty FTE. This type of incremental growth is consistent with what one would expect from a dynamic department in a burgeoning field. It is doubtful that the Novartis Agreement had very much to do with this development except in so far as it provided start-up resources that facilitated successful recruitments. The situation with respect to PMB's allocation of campus space can be gleaned from Figure 4. At the end of AY2000-2001, the Department actually had somewhat less laboratory space, as well as less total assigned space, than it had had in AY1997-1998.

[13] During 1998 there was talk of Novartis providing an additional $25 million for construction of a research facility on or near the campus. However, no formal commitment of this amount of support for capital improvement was ever made.

Figure 4

PMB: Campus Space Allocation



	'94-'95	'95-'96	'96-'97	'97-'98	'98-'99	'99-'00	'00-'01
Research	46.534	46.534	53.232	54.493	55.405	52.014	51.881
Total Space	76.403	81.982	89.337	91.11	89.54	86.822	86.077

RESEARCH DIRECTIONS

Would the Novartis Agreement affect the nature of university research? This was probably the most frequently raised issue at the time the Novartis Agreement was signed. It has persisted in the media ever since.

". . . should we allow commercial forces to determine the University's educational mission and academic ideals? In higher education today corporations not only sponsor a growing amount of research—they frequently dictate the terms under which it is conducted."[14]

The Kept University

"[PMB might be] 'bent' away from the research of the university and toward more applied activities."[15]

(CAPRA, COR, AF)

"Are we effectively subsidizing research for industry? How will we assure that the [Novartis] money will fund 'public good' research?"[16]

(DIVCO)

"Did the Novartis contract turn environmental researchers into handmaidens of industry at the expense of critical research?"[17]

(State Senator Tom Hayden)

Most of commentary on the potential research impact of the Novartis Agreement can be distilled into three propositions:

- Reliance on a profit-driven enterprise for major funding would deflect PMB researchers (faculty, students, post-doctoral fellows) from conducting basic research and pull or push them toward doing research of an applied nature i.e., research designed to have a direct commercial use and payoff. This has been the primary concern, but secondary concerns have also been raised:
- PMB faculty would become dependent on the "easy" grant money obtainable through the "in-house" Novartis review process, and, as a result, become less likely to apply for funding from other external funding sources.
- A closely related concern was that, as a result of the availability of "in-house" Novartis research money, PMB research would not be "peer reviewed." Consequently, it would not be subject to the type of competitive scrutiny that many see as central to maintaining the quality of modern science in the U.S.

---

[14] Eyal Press and Jennifer Washburn, "The Kept University," The Atlantic Monthly, March 2000, pp. 39-53.

[15] DIVCO QUESTIONS, p. 11.

[16] Ibid., pp. 11 and 2.

[17] Letter to President Atkinson, March 21, 2000, p. 2.

The concerns voiced about the impact of the Novartis agreement on the type and direction of PMB's research have been a primary driver of this administrative review. We have treated these concerns and their anticipated impacts as hypotheses to be tested. Have PMB faculty become overly reliant on Novartis funding to support their laboratories? What has been the record of PMB faculty with respect to obtaining non-Novartis funding for their research? Has the nature of what the PMB faculty study changed since their Department entered into the "strategic alliance" with Novartis/Syngenta? Has PMB research become more applied, or more oriented to commercialization, than before the Agreement? What of the research projects that have received awards from the Novartis Research Committee? Are they of the applied or commercial type, or do they represent basic scientific inquiry?

Research Support—Dependency or Diversification

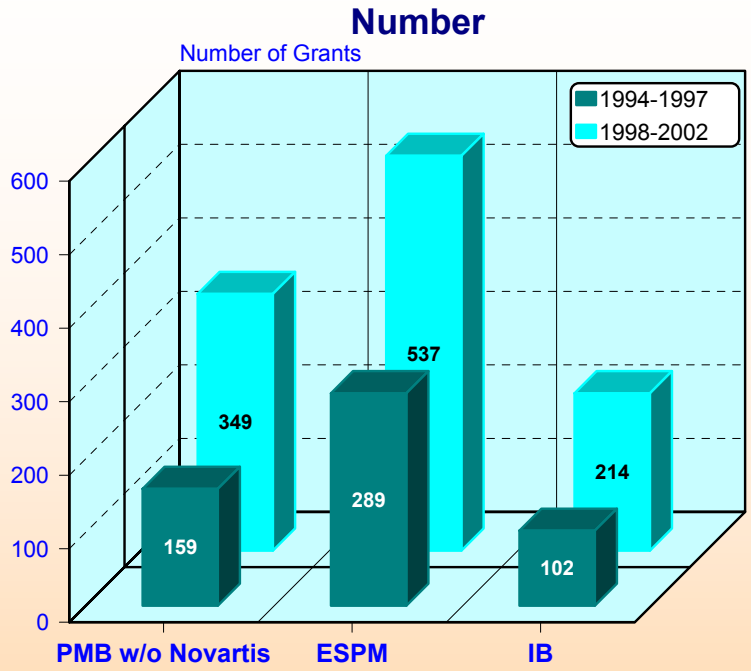
Our examination of the research activities of the PMB faculty since the University entered into the Novartis Agreement in November of 1998 indicates that Novartis funding has not had the adverse impacts on research that have concerned many on our campus and beyond. Figures 1 and 2, already discussed, which show that Novartis provides less than one-third of PMBs research funding (27 percent), provide some indication that the PMB faculty has not become overly dependent on Novartis for its research support, but have, instead, been quite active and successful in obtaining extra-mural funds from non-Novartis and non-industry sources. Figure 5 provides more direct evidence on this matter. It compares PMB extramural research funding in two four-year periods—the four years prior to the Novartis Agreement and the four initial years of the Agreement's implementation. The Novartis Agreement funds are excluded from the displayed data. Figure 5 also provides a comparison of the grant-record of PMB faculty and that of two other academic departments—Environmental Science, Policy, and Management (ESPM) and Integrative Biology (IB).

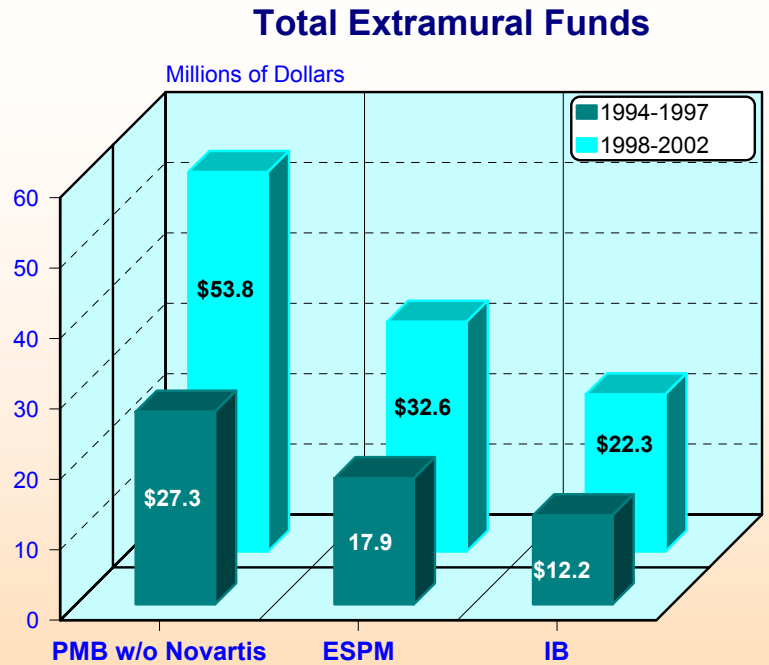
It can be observed that during the period in which the Novartis Agreement has been in effect, the faculty of PMB did quite well in obtaining grants beyond what was available to them through the Novartis/Syngenta connection. The number of grants obtained increased from 159 to 349, a jump of 119 percent. The total research dollars raised went from $27.3 million in 1994-1997 to $53.8 million (with $20 million of Novartis money excluded[18]) in 1998-2002, an increase of 95 percent. The percentage increase in both number of grants and total research dollars, 119 percent and 92 percent respectively (with Novartis funding excluded), was larger for the PMB faculty than for the faculty of ESPM or IB. The fourth graph in Figure 5 adds another comparative reference to the inter-departmental comparison— the Division of Biochemistry and Molecular Biology (BMB) of the Department of Molecular and Cell Biology (MCB). It can be seen that PMB's percentage increase in non-Novartis extramural funding during the Novartis years exceeded that of the BMB, as well as that of ESPM and IB.

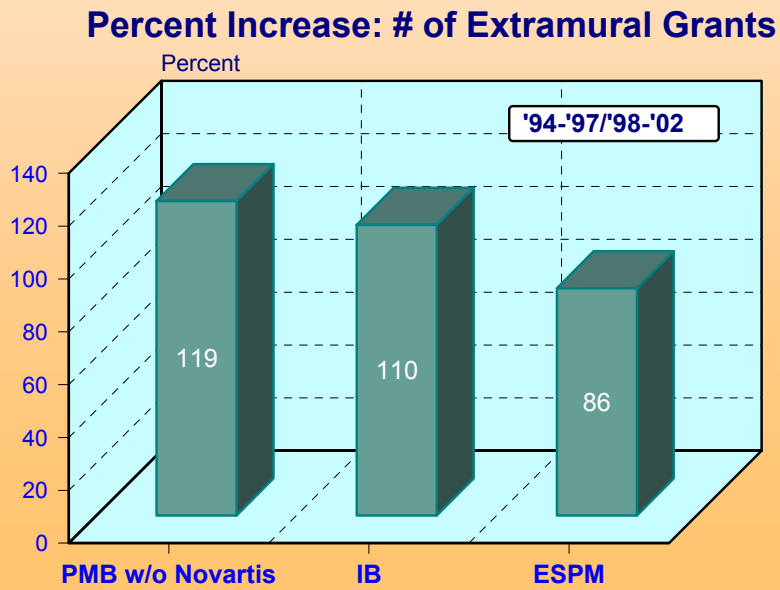
[18] Although the Novartis Agreement is for $25 million over a five year period, the calculation here covers the first four years of the Agreement and so we have calculated the Novartis contribution during that period as $20 million ($5 million X 4).

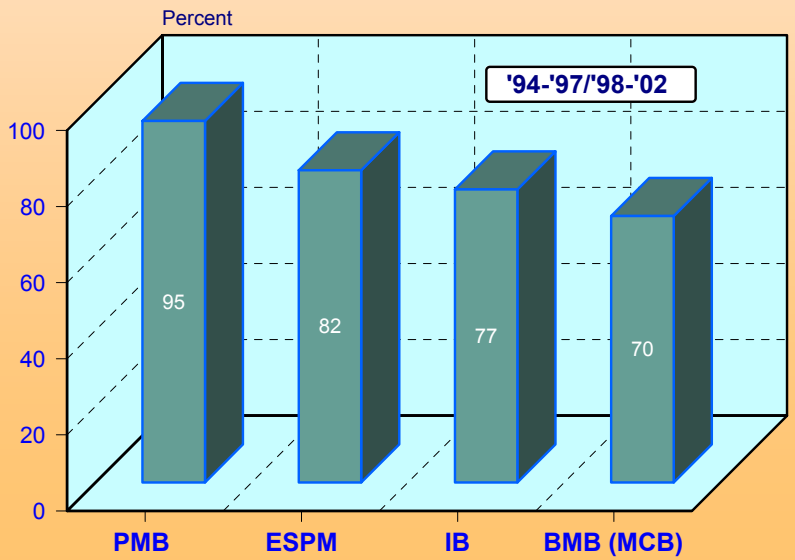
Figure 5

Extramural Grants (Novartis excluded): PMB, ESPM, IB









In order to ensure that the grant generating performance of PMB compared with the other departments is not merely a function of departmental size, Figure 6 displays grant generating performance in per capita, or per faculty member, terms. It can be seen that during the initial four years of the Novartis Agreement, PMB was obtaining an average of 13.4 grants and $2.02 million per member of the faculty. In both respects, PMB outperformed ESPM and IB by a considerable margin.

PMB's success in obtaining extramural research support from non-Novartis sources includes success in peer reviewed competitions. While not all the grants obtained either before or after the Novartis era were peer reviewed, many have been. During the Novartis years, PMB faculty succeeded in receiving some 157 grants, in total, from federal agencies that characteristically award research grants on a peer reviewed basis (NIH, NSF, and USDA). The number of grants from these sources actually doubled during the Novartis years (1998-2002) compared to the four year period preceding the Agreement. Figure 7 shows this increase in peer reviewed funding from Federal Government agencies.

The record is clear with respect to the concerns that PMB would become dependent on Novartis for its research support and that it would become removed from the rigors of peer-reviewed competition. The PMB faculty has maintained a diversified portfolio of research sponsors; it has achieved marked success in increasing the number of its extramural grants as well as the total inflow of extramural research dollars; and it has continued to bring in grants through peer reviewed competitions. But what of the direction of the research being conducted? Has Novartis sought to shape the kind of research that is undertaken? Has it pressured PMB faculty, directly or indirectly, with respect to the type of scientific questions they study? Has there been a shift toward applied, or commercial, research? Here the focus is on matters related to the **continuity** and **content** of PMB's research program.

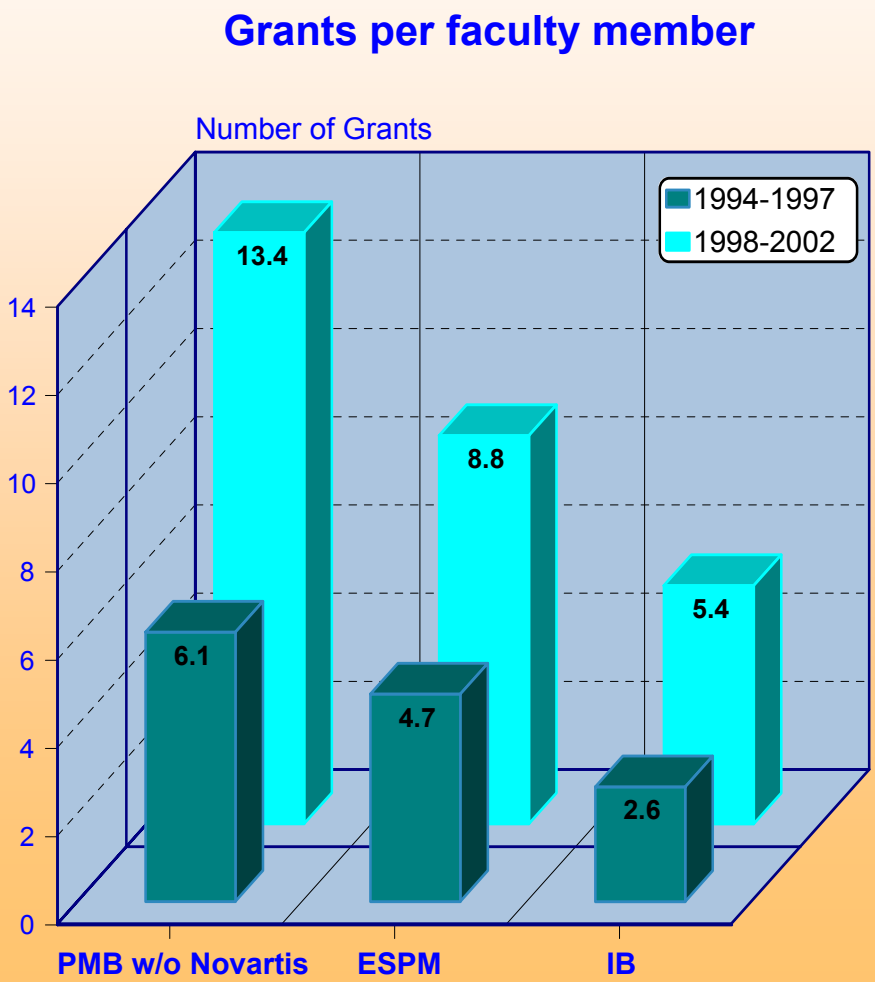
Foci of Inquiry—Continuity or Change

Each of the PMB faculty interviewed in the course of this review was asked how the Novartis Agreement affected their research, what changes they had noticed in PMB's research agenda, and whether they thought that the Agreement had led to more commercialized/applied research as opposed to basic research. Every one of the eighteen faculty members that we spoke with insisted that nothing had changed in the fundamentals of the science being conducted in their department. They were each adamant that the research being conducted in their labs, both with Novartis and non-Novartis funds, represented an extension of scientific inquiries in which they had been engaged prior to the Agreement. The faculty members we interviewed felt that the Agreement has assisted them in improving their methodology and in pursuing their scientific inquiries in new and novel ways. Not a single faculty interviewee felt that the Novartis Corporation or its research arm, NADII/TMRI, had attempted to influence them

Figure 6

Extramural Grants per faculty member: PMB, ESPM, IB

Number and Total dollars



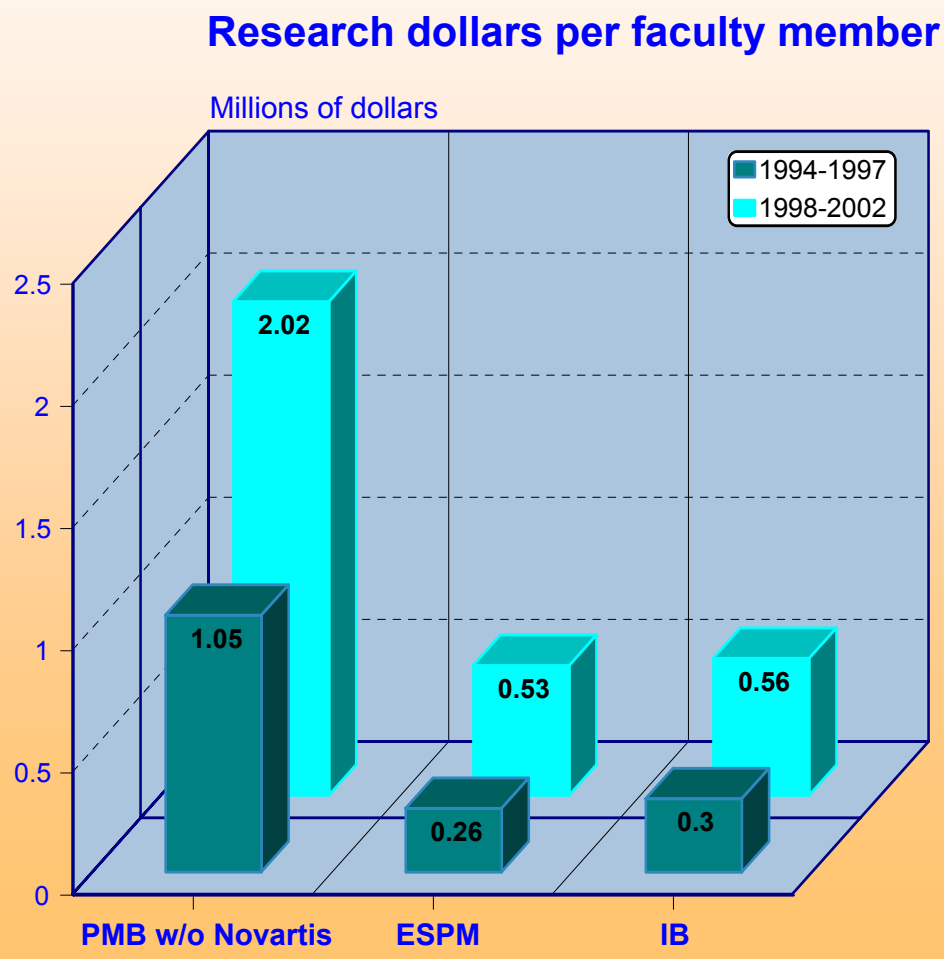
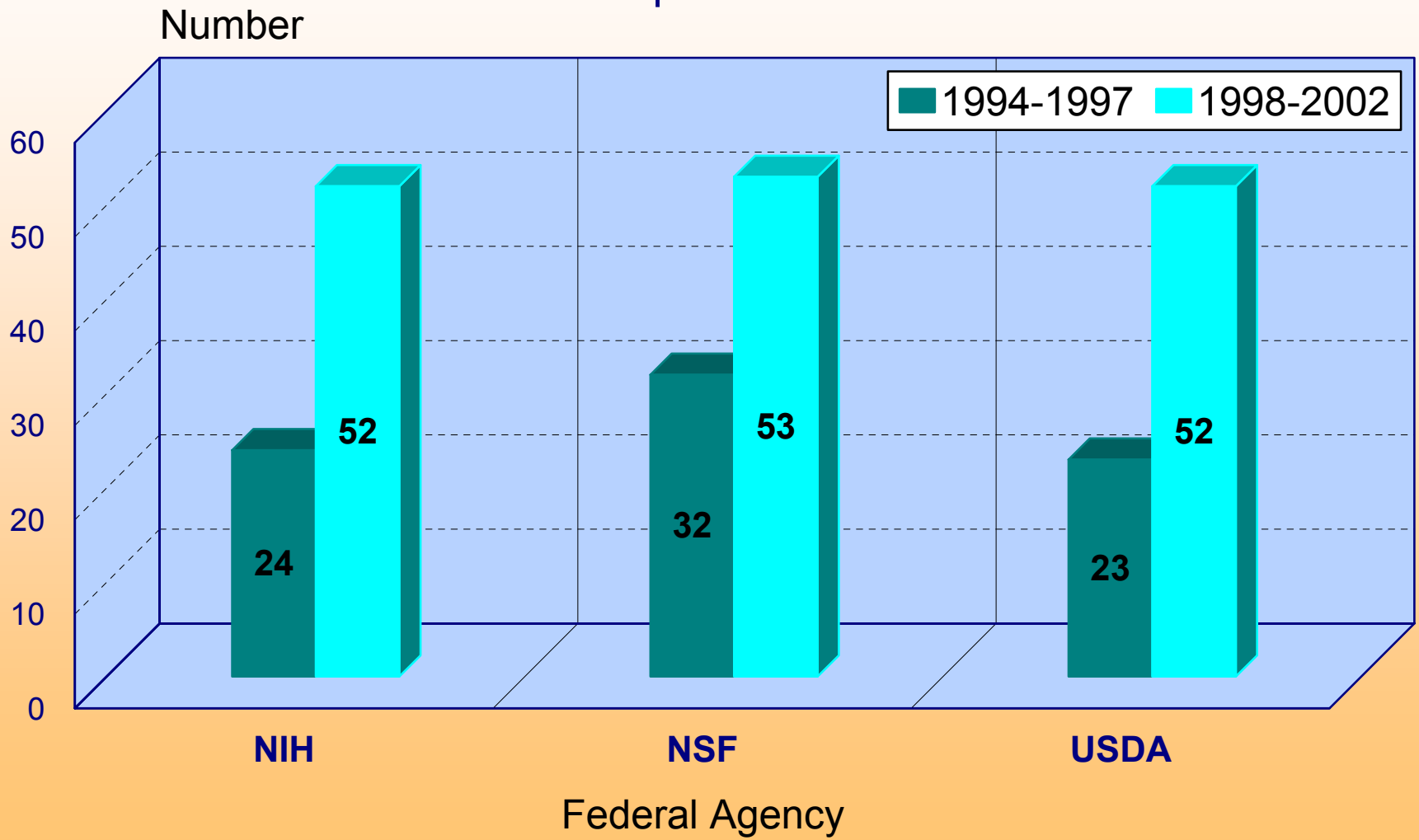


Figure 7

Federal Agency Grant Competition

Number of grants obtained: PMB Faculty

1994-1997 compared to 1998-2002



Data source: Sponsored Projects Office

in any manner with respect to what research question they should study. Neither were they aware of any colleagues who felt that they had been the subject of such attempts.

With respect to access to Novartis Agreement research funds, the faculty we interviewed commented on both the ease and openness of the process whereby Novartis funds were allocated to departmental faculty and their laboratories. They took particular note of the fact that they were able to receive funding without having to clear the array of substantive and bureaucratic obstacles that have come to characterize the scramble for extramural grants. They each emphasized that the Novartis funding process was completely open with respect to the content and subject of their research— i.e., the funding criteria applied by the Research Committee places no constraints on what might be studied, and no justification with respect to linking research requests to practical applications is required. None of the interviewees had been asked by the Research Committee to alter their research focus or methodology, and they were not aware of any instance in which such alteration had been requested, either by the Committee as a whole or by the Novartis representatives on the Committee.

Several interviewees pointed out that Novartis funding is less encumbered than funding provided by federal agencies, since the latter almost always require applicants to indicate the practical or social impacts of their proposed research. NSF, for example, evaluates proposals based on two "merit criteria," one of which is intellectual merit and the other is "the broader impacts" of the proposed research. NSF explains that an element of the latter criteria is "benefits to society," and in explaining to proposers how they might meet this criteria states: "The knowledge provided by NSF-funded projects offers a rich foundation for its broad and useful application. For example, projects may contribute to understanding the environment, commercial technology, public policy, health or safety and other aspects of public welfare."[19] The Novartis Agreement contains no similar stipulation with regard to the distribution of research funding, and, as far as we are aware the Research Committee has not applied either a social or commercial impact criteria.

In order to test the faculty's claim of research continuity, we compared the focus of journal articles published by the PMB faculty in the years preceding the Novartis Agreement with the scientific focus of the twenty-three research programs funded by the Research Committee. Curricula Vitas provided title information with respect to the faculty's publications, and hence an indication of their subject matter; project abstracts, issued by the Research Committee for each of its funded research programs, provided a basis for judging the subject matter of research supported by the Novartis Agreement. In each of the twenty-three cases, the PI's Novartis-supported research focused on an area of science about which the PIs had published, often numerous times, in the years preceding the Novartis Agreement. On the basis of the testimony of the PMB faculty, corroborated by an examination of the publication record of each faculty member, it is reasonable to conclude that the PMB's research agenda remained fundamentally unchanged by the Novartis Agreement.

[19] National Science Foundation, "Merit Review Broader Impacts Criterion: Representative Activities," pp. 1 and 4-5.

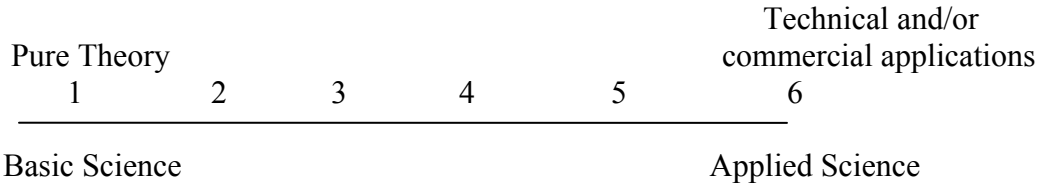
Although there has been a good deal of continuity in the subjects of PMB research and the lines of inquiry pursued by its faculty, there is one area in which the Novartis Agreement has facilitated a marked change—the field of genomics within PMB has been enhanced. Funding made available through the Research Committee as well as access to TMRI's genomic bioinformatics database, microarray equipment, and computer software, has made it possible for those already doing genomics to enhance and expand their studies, and, for those who had not previously been so involved, to incorporate genomics as a component of their research program. Both faculty members and graduate students spoke very positively about how the opportunities made available by the Agreement facilitated their learning of new research technologies and methodologies in the areas of genomics and bioinformatics. They considered that, as a result, they and their colleagues were doing better science.

It should be noted that while the stated purpose of the Agreement, to advance research in agricultural genomics, has been achieved, the Research Committee has funded research that is "non-genomic," as well. We found no evidence that Novartis had "targeted" its research money toward either genomics in general or specifically toward genetic research linked to the corporation's commercial interests.

Basic or Applied Research?

The above discussion of continuity in PMB's research agenda suggests that the Novartis Agreement has not moved the department significantly toward more applied and less basic science. However, the proposition that the Novartis Agreement would bend PMB's research agenda toward applied and even commercial purposes can also be directly addressed.

The determination of whether scientific research should be consider basic or applied is a vexing matter since what is commonly presented as a dichotomy—basic vs. applied research—is in actuality a continuum. At one end of this continuum, the basic end, is pure theory. At the other end of the continuum, the applied end, is the creation of a usable and potentially marketable product. In between are degrees of 'basicness' and 'appliedness'. We can think of basic research as directed to creating knowledge and



applied research as directed to creating products or technical applications, but that does not help us much in escaping our conundrum. For, the creation of virtually any product will depend on the existence of prior knowledge (i.e., basic science), and virtually any basic scientific knowledge can, with some imagination, be conceived as having implications for productive development somewhere down the scientific, engineering,

and technical trail of discovery. The best we can do, then, is to think in terms of a continuum on which scientific research can be arrayed in terms of its proximity, or lack thereof, to the creation of a usable product.

What can be said about research in PMB, both before and during the Novartis Agreement, is that its laboratories occupy somewhat different positions in the middle sector of the above continuum—say between 2.5 and 4.5. None of the PMB labs is concerned with pure theory, and none is involved in product development.

One of the concerns expressed about Novartis's involvement with the University is that it would use its funding to promote commercial research by the PMB faculty. An examination of the research abstracts for each of the twenty-three Agreement-supported research projects (See Appendix A) reveals that none of the research being supported by Novartis funding is commercial in nature. All the PMB laboratories are doing basic science. In some the basic science is focused on a research problem that could well produce knowledge that might assist in the development of a practical application and possibly a commercial product—e.g. the genetic aspect of plant disease. Such a lab would be located closer to #6 on the above continuum than a lab whose basic science produces knowledge whose practical application may well exist but is less obvious. Examples of both types of research projects supported by Novartis funding can be found in the abstracts reproduced below:

> Antje E. M. Hofmeister, "Mechanism of signal transduction for the proteolytic activation of a developmental transcription factor"
>
> The goal of this project is to characterize the function of the putative receptor/protease SpoIIGA in the signal-dependent proteolytic activation of the developmental transcription factor s^E. The SpoIIGA protein is required for the proteolytic processing of pro-s^E to the mature s^E factor, which is crucial in establishing cell-type-specific gene transcription early during spore development in the soil bacterium *Bacillus subtilis*. Our investigations are directed at characterizing the extent and the nature of the interactions of SpoIIGA with pro-s^E, SpoIIR, and as yet unknown additional proteins. In addition, we will determine the functional consequences of these protein interactions on pro-s^E processing and on compartmentalization of s^E activity. Elucidating SpoIIGA function and its regulation during spore development will advance our understanding of the cellular processes that redirect protein constitution in response to extracellular signals during formation of specialized cell types.
>
> Steven Lindow, "Disruption of microbial extracellular signalling systems as a novel method of plant disease control"
>
> Plant pathogenic bacteria live on plant surfaces before causing disease. We have found that the survival of such bacteria on leaves is dependent on their ability to communicate with each other by means of small molecules called N-acyl homoserine lactones (HSLs). We are cloning the genes for the production of such

molecules from the bacterium *Pseudomonas syringae* and are exploring the possibility that the signaling process can be disrupted in the presence of analogs of such signaling molecules. We will produce a variety of HSLs in transgenic plants and determine if they can alter the survival and disease-causing potential of this species. Our goal is thus to control disease through the natural production of bacterial signal molecules so that pesticides such as antibiotics can be avoided for disease control.

The Lindow project, above, clearly involves basic science while at the same time it focuses on an issue in which the discovery of new knowledge would appear to have fairly clear implications for developing practical applications. Such implications appear to be less obvious in the basic science conducted by Professor Hofmeister. Hence, both research projects can be considered to be conducting basic science, although the Lindow project appears to have more medium-term applied implications. A perusal of the abstracts for each of the Agreement supported research projects (Appendix A) shows that Novartis funds have supported both types of projects. There is no indication that Novartis tried to influence PMB research toward the Lindow type of "applied" project. Even if it had, it would only have been doing what all federal agencies do in their research competitions. Moreover, it is doubtful that the critics of the Novartis Agreement have actually been concerned about this form of mixed "basic-applied" science. Rather, their worry was that Novartis, as a profit driven business enterprise, would pressure PMB into conducting directly practical and, in particular, commercial research. As already noted, there is no evidence that this has happened, and considerable evidence that it has not.

The type of journals in which PMB faculty publish provides an indirect measure of the kind of research they conduct. Are these journals publishing basic science or are they oriented toward reporting practical, technical, or commercial applications? If the Novartis Agreement is shifting PMB research away from basic science that trend should be reflected in a corresponding shift in publishing outlets. We examined the *curricula vitae* of each PMB faculty member so as to tabulate the location and publication rate of their journal articles during the four years preceding and the four years after the Agreement was signed. Since the date of journal article publication lags behind the time in which the reported research is actually conducted, this represents a rather crude indicator of research differences in the two time periods--i.e., research published in the 1998-1999 academic year could well have been completed in the 1997-1998 academic year. However, if there has been a significant shift in the type of research being conducted by PMB faculty it would probably manifest itself in publications by the later years of the Novartis-PMB relationship and therefore ought to be reflected in our tabulation.

During the eight year period we examined, PMB faculty members have published articles in some 36 journals. All of these journals are devoted to publishing the results of research in basic science. They differ with respect to sub-specialty, but none of them is an outlet for commercial or directly applied research. The number of articles published increased from 206 in the 1994/95-1997/98 period to 232 in the

1998/99-2001/02 period, but the same nine journals publish the bulk of PMB articles in both periods (72 percent and 66 percent, respectively). The four or five most prestigious journals for plant scientists are among this group of nine. The distribution of articles among them is presented in Table 1, below.

Table 1
PMB Faculty Articles
Selected Journals

Journal	*'94/95-'97/98*	*'98/99-'01/02*
Genetics	10	11
J. of Bacteriology	13	12
Plant Cell	28	26
Plant Journal	16	18
Plant Physiology	20	28
Planta	13	9
Proc. Natl. Acad. of Sci (PNAS)	21	38
Science	11	4
Virology	17	8
Total: All Journal Articles	206	232

While disputing the claim that Novartis support pushed PMB research in a more applied direction, the faculty members interviewed for this report, to a person, describe what they consider to be a strengthening and improvement in their already existing research program. Two things are stressed: First, they argue that the manner in which the Research Committee has distributed Novartis funds has allowed them to pursue more innovative and more creative lines of inquiry than would have been supported by alternative funding sources. Several of those interviewed describe what Novartis funding has made possible as "blue sky research." The view we heard over and over again was that the grant proposal review process administered by the major federal funding agencies is inherently conservative in the sense that it favors research whose results are likely and predictable. They point out that obtaining such grants requires a "track record" of experimental results, such that much of the foundational research must already be completed. Hence, the process makes it difficult, if not impossible, to strike out in new directions and to try something really innovative. In the view of the faculty participants, the Novartis Agreement, and the operation of its Research Committee, has had the opposite effect, offering them multi-year grants to follow lines of inquiry that otherwise they would have been unlikely to be able to pursue. In a typical comment, one faculty member described Novartis funding as "seed money to do really new, novel and innovative things." "I would not have had the background data and track record to have received federal funding for this research," he said. "Now, based on my Novartis funded research, I am submitting a large NSF grant proposal, and stand a good chance of success."

The second contribution stressed by the faculty interviewed is the cost-free access that interested PMB faculty members have obtained to the Novartis/Syngenta/TMRI proprietary genomic bioinformatic database and related technology and research tools. The collaborative relationship with TMRI offers PMB researchers a means for studying gene expression on a genome-wide scale. They can utilize TMRI's custom designed GeneChip® arrays for rice, *Arabidopsis*, and maize cDNA, as well as a number of commercial GeneChip® arrays. Their gene expression analysis can be done at the TMRI's facility, utilizing a GeneChip® microarray system that includes a fluidics station, a high-resolution scanner, a controlling computer, a hybridization oven, and software designed for image processing, visualization, pattern recognition, and statistical analysis.

Those PMB faculty members that have made use of the TMRI database and facilities describe a situation in which without the Agreement their current research would have been either impossible, because the relevant data was not publicly available, or prohibitively expensive. A member of the faculty working on the functional genomics of *Arabidopsis* describes the Novartis Agreement as "providing me with expensive tools and services at no charge (bioinformatics, beta analysis, gene chips, scans) which the federal government would never fund and which I could otherwise not afford."

Finally, faculty members report that the Novartis funding enhanced the research capability of their laboratories by providing the means to recruit post-doctoral scholars and top-flight laboratory managers that otherwise they would have lacked the resources to employ.

For many of the critics of the Novartis Agreement, their concerns have been less about basic versus applied science than about biotechnology as a field of scientific inquiry. From the outset, the Agreement has been enmeshed in the highly contentious debate over bio-technology in general and genetic modification of food, in particular. Concerned about unknown potential dangers of genetically engineered food, some have opposed any research related to genetic engineering, especially if it is funded by those who have a financial stake in producing genetically modified organisms. More moderate critics worry that the research funds made available to university scientists by industry will result in an imbalance in University research, with non-genomic science and technologies that are alternatives to bio-engineering being dwarfed. Of course, on the other side of this debate are those who argue, just as strenuously, that genomics represents the frontier of modern biology; that bio-engineering has powerful potential benefits for humankind; and, that whatever risks exist can be known and controlled. Hence, what would be considered by one side of this debate as an adverse consequence of the Novartis Agreement—the expansion and advancement of genomics within PMB—would, to the other side, appear as a major benefit. In this review we do not enter into this debate by judging the value of genomics and bio-technology. Rather, our concern is simply to discover what effect, if any, the Agreement has had on PMB with respect to this area of science.

Research Collaborations

At its inception, both the PMB faculty and the Novartis Corporation appear to have envisioned that the Agreement would lead to active research collaborations of a "joint" nature between Berkeley and Novartis scientists. This is reflected in the language of the Agreement, which speaks of "joint research contemplated by this Agreement," by mention of Novartis's intention to establish a research facility near the Berkeley campus, and by reference to possible appointments of Novartis employees to University academic positions (as Adjunct Professors). Interviews with PMB faculty members indicate that they looked forward to an interactive relationship with Novartis scientists in the pursuit of joint research.

Although for the PMB faculty the collaborative nature of the Novartis Agreement held considerable promise, for others, and especially for the Academic Senate, it raised a number of serious concerns. The latter worried that such collaboration would create an industry presence on the campus that would be too heavy and too intrusive. Specifically, they were concerned that a significant number of Novartis scientific personnel would be housed on the campus, occupying all too scarce University office and laboratory space. They also worried that industry scientists would be appointed as Adjunct Professors and potentially impinge on the faculty's role in departmental governance, curricula development, and graduate student mentoring and supervision.

The actual experience of the Novartis Agreement with respect to research collaboration has been somewhat different than what was anticipated by some. There appears to be less direct interaction between Novartis and PMB scientists (faculty, graduate students, and postdoctoral fellows) than was envisioned early-on. Although several of the PMB laboratories have engaged in interactive collaboration with TMRI colleagues, for the most part the interactive aspect of the PMB-TMRI relationship has been confined to an annual retreat in which PMB faculty, as well as some Berkeley graduate students and post-doctoral fellows meet with scientists from TMRI to discuss their current research endeavors and progress. PMB faculty members we interviewed found these annual retreats to be a very worthwhile experience. In a few instances contacts were made that already have, or might soon, evolve into research collaborations. No Novartis personnel have worked in campus laboratory facilities with their Berkeley counterparts. No industry scientists have received appointments as Adjunct Professors.

Intellectual Property

At the time the Novartis Agreement was signed, concerns abounded about control over the intellectual property generated by PMB research, and about the freedom of PMB researchers to publish or otherwise disseminate their research. The perceptions that gave rise to these concerns have generally persisted, as can be seen in a recent magazine article, authored by a UCB faculty member, who states: "The Novartis deal caused controversy primarily because it demanded that Berkeley researchers sign

confidentiality agreements."[20] The myriad concerns related to intellectual property matters can be grouped into three "issue areas."

- Secrecy
- Patent Rights
- Publication Delays

Does the Novartis Agreement require PMB researchers to maintain secrecy or confidentiality with respect to research they conduct? Are PMB faculty and graduate students required to sign confidentiality agreements in order to receive funds from the Research Committee? This type of frequently voiced concern would appear to rest on a persistent and basic misperception-- that participants in the Novartis project are required to sign confidentiality agreements. **It is not the case, however, that PMB participants in the Novartis-PMB program and/or those who receive Novartis funding from the Research Committee, are required to sign a "confidentiality agreement" regarding their research.** No such general or blanket confidentiality arrangement is required by the Agreement and no such arrangement has been entered into since the Novartis program was initiated.

The matter of confidentiality arises only with respect to the genomic bioinformatic database and related microarray technology which Novartis considers proprietary. If a PMB researcher wishes to use Novartis's gene chips and microarrays in his or her experiment, then the researcher must sign an agreement not to disclose to a third party the underlying genomics bioinformation, technology, and methodology supplied by Novartis and utilized in the gene expression analysis. This does not preclude the reporting or publishing of the research results obtained through such analysis.

In sum, within the Novartis Agreement the matter of confidentiality is circumscribed, relating only to information that Novartis owns and that is unavailable from other sources. Non-disclosure agreements are entered into voluntarily-- only those who choose to access Novartis's proprietary database need sign them. A total of eleven faculty members have signed such agreements, along with the students and post-doctoral fellows working with them on their projects. Those PMB faculty members who have not utilized the Novartis genomic database or research tools, and therefore have not signed non-disclosure agreements, have nonetheless received Novartis funding for their research projects.

Another highly controversial aspect of the Novartis Agreement has been the clause that gives Novartis the first right to negotiate a license on a portion of patentable discoveries ("research inventions") made in PMB laboratories, whether or not the discovery was made with Novartis funds. The portion available to Novartis is based on a ratio of Novartis-supplied funding to other non-commercial research support received by PMB.

[20] David Kirp and Elizabeth Berman, "A Good Deal of Collaboration," California Monthly, September 2002.

During the course of the agreement this has meant that Novartis has an option to license approximately one-third of all the research inventions made in PMB laboratories. [21]

In assessing this aspect of the Novartis Agreement, several things should be noted at the outset. First, the University retains ownership to all PMB research results and has the right to copyright, publish, disclose, and disseminate them. It has not relinquished either ownership or these associated rights to Novartis, except, as noted above, when the research results contain Novartis's proprietary information. In that case, either Novartis must approve publication or the references to proprietary information must be removed. Second, Federal law and University regulations require researchers to disclose research inventions.[22] It is common practice for the campus's Office of Technology Licensing (OTL), once an invention disclosure has been made, to search for a private sector firm that will commit to further develop and commercialize the invention and pay the costs associated with patent filing (anywhere from roughly $2,000 to $15,000). In return for such a commitment, the firm receives an option to negotiate a license that provides access to the University's patented invention. Hence, granting to Novartis the first right to negotiate a license alters little in common practice except to "eliminate the middle-man," i.e., the OTL need not go out and find a firm interested in financing a patent filing, unless Novartis determines it is uninterested.

Between November of 1998, when the Agreement came into effect, and August of 2002, Novartis has had the option to negotiate a license on six research inventions (there were 16 research inventions disclosed by PMB faculty during this period). It exercised its option on four of these inventions, but declined to go forward with licensing on three of them. Thus, over the first four years of the five year Agreement period, Novartis has retained an option to negotiate a license for one PMB research invention. It should also be noted that Novartis/Syngenta has underwritten the cost of patent applications and paid option fees to the University for all four of these inventions, including the three that it ultimately decided not to license. To date, this has involved $131,250 in reimbursed patent costs and $50,000 in fees.

Concerned about maintaining the free flow of scientific information, Academic Senate committees worried that Novartis would be able to delay or even prevent PMB's faculty, graduate students, and post-doctoral fellows from publishing the results of their research. While there is nothing in the Novartis Agreement that can prevent the publication of PMB research, there are several provisos that could delay the dissemination of research for specified and limited periods. All PMB researchers participating in the Agreement are required to provide Novartis with a preliminary draft of their intended research publication or presentation thirty days prior to its submission for publication or other form of dissemination. The purpose of this proviso is to allow Novartis to assess whether

[21] Novartis's first right to negotiate licenses for a portion of PMB inventions ceases when the Agreement terminates at the end of five years.

[22] See, Office of the University of California President (UCOP), "The Bayh-Dole Act: A Guide to the Law and Implementing Regulations," p. 4; and, UCOP, "Statement of Policy: Patent Responsibilities and Administration," October 1, 1997, p. 2.

there are patentable inventions contained in a publication and/or to review publications for inadvertent disclosure of proprietary information.[23]

It should be noted that a period of delay in publication is common practice following the disclosure of a research invention. Researchers disclosing an invention will usually want to prevent the dissemination of their discovery until protection can be obtained through the filing of a patent application. This application process can take anywhere from several weeks to several months, depending on the complexity of the invention and the amount of information made readily available to the patent attorney. In addition, the inventor will usually seek to limit the dissemination of their discovery while they search for an industrial licensee. As already noted, when a University researcher discloses a research invention to the Office of Technology Licensing (OTL), it will seek an industrial licensee who will commit to further develop and commercialize the invention. Since potential licensees need access to the invention in order to determine whether they have an interest in it, the University will usually require a "secrecy" agreement from them so as to protect the researcher's discovery from dissemination to third parties. According to the Annual Report of the University of California Technology Transfer Program in FY00 "959 secrecy agreements were executed [within the UC system] that enabled companies to receive confidential information necessary to evaluate campus inventions for commercial potential. In sum, delays and limits on the dissemination of research results are a common feature of the process whereby inventors and the University seek to obtain patents on discoveries from campus research. They are not something peculiar to the Novartis Agreement.

None of the twenty-five PMB faculty, graduate students, and post-doctoral fellows we interviewed considered the thirty day publication delay imposed by the Agreement to be a significant problem. One faculty member referred to it as a "minor inconvenience." The pre-publication procedure was described as simple and unobtrusive. In essence, those we interviewed offered the following description of their experience: they provided Novartis with a manuscript draft prior to the time they were ready to submit their papers for publication; they would have probably taken at least thirty days to finalize their drafts; and, thus, the thirty day publication-delay imposed by the Agreement was, in actuality, no delay at all. Only one of those we interviewed had experienced any objections from Novartis about their intended disclosure of information. In that instance, a postdoctoral fellow preparing to make a conference presentation presented a précis of the presentation to Novartis, was told that some of the information in the presentation was proprietary, and was asked by Novartis to make modifications so as to avoid such disclosure. According to this postdoctoral researcher, Novartis's suggestions were easy to implement and did not appreciably alter the substance of her conference presentation. She did not consider her experience to be problematic.

If, after assessing the draft submitted for the thirty day review, Novartis decides that the report of research results contains potentially patentable material, it has up to 90 days to

[23] Amendment #1 to Collaborative Research Agreement No.: 010134, Articles 9 and 10; see also, "Collaborative Research Agreement—Condensed Version, November 12, 1998 p. 5 ; and, "PMB-NADII Collaborative Research Agreement, Guidelines for Publication Procedures," March 2, 1999.

request a patent application by the University before the invention can be published. Hence, it is possible that the publication of results of research conducted in a PMB laboratory could be delayed for a total of 120 days (30 days for the initial review plus 90 days to allow for patent filing). However, if publication is desired by the inventor more rapidly, the University will, on its own, file a "fast track" patent application (approximately 14 days), after which dissemination of results can take place without jeopardizing patent protection. As a matter of practice**, none of PMB's research results have in fact been subject to this 90 day delay**.

In sum, we have found that in its operation the Novartis Agreement has had at most a minimal impact in the area of intellectual property concerns. Non-disclosure, or confidentiality, has been applied only in a circumscribed area— Novartis's proprietary genomics bioinformatic database and related technology. Publication delays have been minimal and are considered by faculty to be at most a minor inconvenience. Our interviewees indicated to us that, since they are required to submit only preliminary drafts, the thirty-day pre-publication "rule" did not actually delay publication at all. It would have taken, they note, at least thirty additional days for them to have completed writing the paper in question. Although the Agreement allows for publication delays to be extended from 30 to 120 days, such a delay has not occurred in the four years that the Agreement has been in effect. Finally, Novartis has shown rather limited interest in licensing PMB research discoveries.

We recognize that the university-industry relationship, as it affects intellectual property matters, engages significant issues of principle and philosophy. It is argued by some, for example, that as a matter of principle it is wrong for universities to allow any agency, and especially an external one, to require confidentiality agreements and publication delays. The fact that, as a "matter of practice," these have been narrow in scope and limited in duration can not be viewed as an effective counter to arguments about **"**matters of principle." As this review of the Novartis Agreement has focused on matters of practice, the philosophical issues embedded in university-industry relationships have not been engaged.

Students and Teaching

Concerns that the Novartis Agreement might have an adverse impact on PMB's pursuit of its pedagogical mission figured prominently in the Academic Senate's comments at the time the Agreement was signed. Given the presumed interest of the Novartis Corporation in protecting its proprietary information, Senate committees were uneasy about whether the graduate program could maintain an open academic atmosphere.[24] They were concerned, as well, about whether graduate students would be prevented from publishing their research in a timely fashion.[25] Another area of concern was whether, as a result of the involvement of Novartis scientists as

[24] See Todd LaPorte (Chair, COR), "Summary of critical reactions . . . ," Question 10.
[25] DIVCO QUESTIONS, Q. 12.4, p. 7

collaborators, PMB training and mentoring of graduate student would slip from the faculty. For example, the Senate's Committee on Research asked "To what degree has the PMB Department maintained its control over the direction, scale and progress of graduate students, e.g., to monitor/certify the types of thesis research work done by GSRA's on projects sponsored by Novartis scientists to assure that it would be at least equal in quality to that done with UC faculty?"[26] A related concern was that the Department's attention would be differentially focused on those graduate students working in areas favored by Novartis.[27] The Agreement's influence on graduate student recruitment and enrollment was also raised. While most of the questions surrounding the pedagogical consequences of the Novartis Agreement focused on graduate student training, there were concerns expressed about its impact on the undergraduate curriculum, as well. The Senate Committee on Academic Freedom, for example, inquired as to whether faculty time would be "bought out" by Novartis money so that fewer undergraduate courses would be taught?

We deal first with the matter of the undergraduate curriculum. Note, at the outset, that Novartis funds have not been used to "buy" faculty time, and thus to reduce faculty teaching commitments. Figure 8 shows that during the period of the Novartis Agreement the number of undergraduate course offerings in PMB increased slightly compared to the period preceding the Agreement's implementation. The average number of undergraduate courses offered by PMB in the five semesters prior to the Agreement was 10 while the average in the five semesters after its initiation was 15. (The academic year 1998-1999, the first year of the Agreement, is excluded from this calculation. It is not possible to classify that year's courses as either pre or post Novartis since the offerings may have been scheduled in the previous pre- Novartis year. Also excluded are individual study courses, such as those numbered 199 and 198).

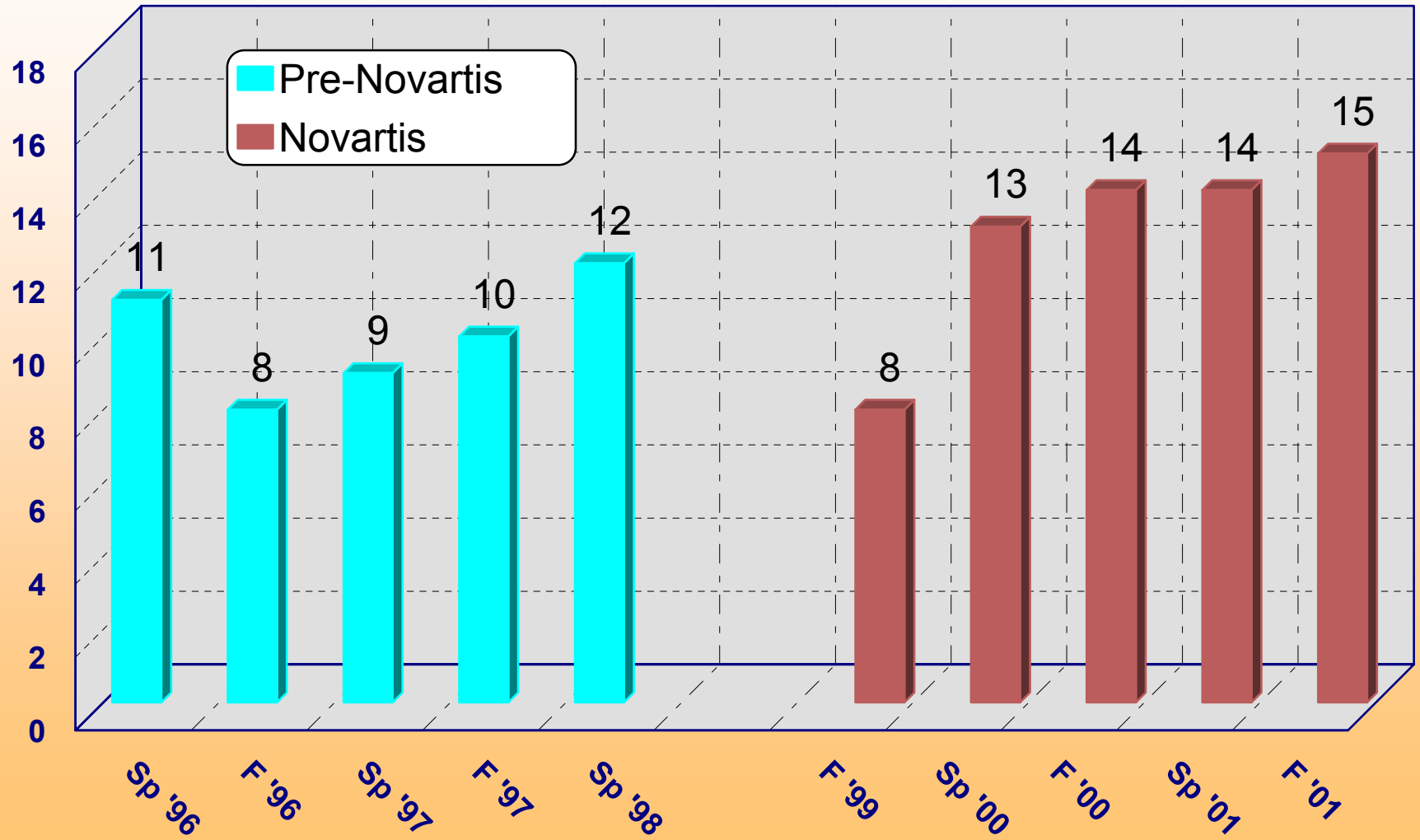
Every undergraduate course that PMB offered in the five semesters prior to the Novartis Agreement is offered in the five post-Agreement semesters, and with the same frequency. The only change that can be observed in the undergraduate curriculum is the addition of several new courses in the years subsequent to the agreement: Fall 1998-- Plants, Agriculture and Society (PB 10); Spring 1999-- Bacterial Pathogenesis (PB C103); Spring 2000-- Biology of Algae (PB 120); Spring 2001-- Microbial Genetics and Genomics (PB 118); Fall 2001-- California Mushrooms (PB 113).

At the graduate level, there occurred a similar evolution in course/seminar offerings. Each of the PMB seminars offered in the pre-Novartis period was also offered in the period after the Agreement's implementation. In the latter period several new seminar offerings were introduced, indicating an expansion of the graduate curriculum in the area of microbial biology and genomics (Critical Thinking in Microbiology, Plant Pathogenic Bacteria, Topics in Genomics and Computational Biology). This type of expansion coincides with the general trend in biological

[26] See LaPorte, op. cit., Q. 12.3
[27] See DIVCO, op cit., Qs. 13 and 14, pp. 7-8.; and, La Porte, Q. 12.3

Figure 8

Undergrad Courses: Pre-Novartis/Novartis*



*honors and independent study excluded

sciences and so there is no reason to attribute it directly to the Novartis Agreement. However, as noted elsewhere in this report, the Agreement has provided PMB with $250,000 per year in fellowship support for students concentrating in the area of Microbial Biology. Hence, the Novartis Agreement facilitated the recruitment and support of graduate students with an interest in microbial biology and genomics.

It is in the area of graduate student support that both the faculty members and the students we interviewed considered the Agreement to have its biggest impact on PMB. In addition to the $3.3 million annually of Novartis funds directly allocated to PMB laboratories, from which graduate student research assistantships are provided, the Department receives $500,000 per year for graduate fellowships. While there is appreciation of the research assistantships, it is the increased fellowship support made possible by Novartis funding that is viewed as really making a difference to the health of PMB. The fellowship money is divided equally between the two PMB divisions—Plant Biology and Microbial Biology-- and awards are made to first and second year students. This aspect of the Novartis Agreement has made it possible for PMB to provide five years of financial support to all its incoming graduate students. As a result, according to the faculty, the Department has remained competitive in the currently fierce "market" for the best graduate student prospects. It should be noted that none of the fellowships funded by Novartis money are "targeted" to students whose research is particularly of interest to industry, as some of the Agreement's critics feared might be the case. According to the Dean of the College of Natural Resources, Novartis money has been intermixed with other fellowship funds, such as the campus block grant, so that there is no link between a particular fellowship and the Novartis/Syngenta Corporation.

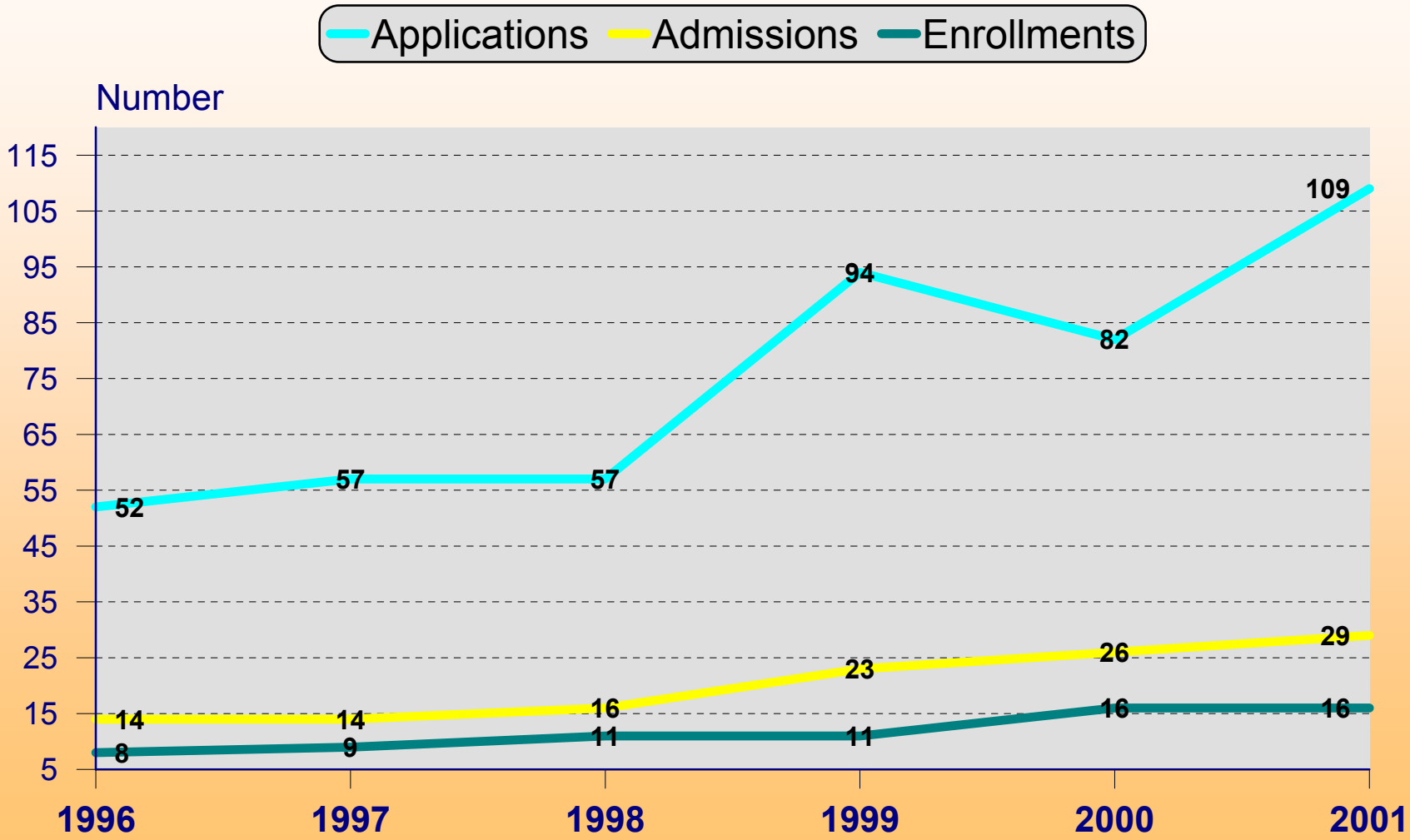
The increase in fellowship funding made available by the Novartis Agreement allowed PMB to expand its graduate program. A concentration in microbial biology was added, and the Department increased the number of graduate students it admits and can support. The changes in this respect are reflected in Figure 9. Since the inception of the Agreement, the number of applications received, the number of applicants accepted for admission, and the number of graduate students enrolled annually, have all nearly doubled.

If, as seems likely, the Novartis Agreement is not renewed, PMB will need to confront having to support its expanded graduate student population. PMB faculty members are confident that current students can be supported on research grants obtained by department faculty and laboratories. However, the department will have to obtain new sources of funding if it is to maintain the size of its annual graduate student intake at the current commitment level of two years of fellowship support for each new student.

It can be inferred from what has already been discussed in this review that the Academic Senate's concerns about possible adverse consequences for graduate education have not materialized in practice. Industry personnel have not played a role in departmental governance, PMB research labs, or in the supervision of graduate training. There is no evidence that any pressure has been exerted on students to

Figure 9

PMB Graduate Admissions



pursue lines of research in which Novartis/Syngenta, or industry in general, is interested. Of the graduate students we spoke with as part of this review, not one had experienced such pressure, or knew of any of their colleagues who had. PMB graduate students are subject to the same publication rules as are the faculty. If they are working in a laboratory of a participating faculty member and they intend to report research results, they are required to submit a short abstract to NADII/TMRI thirty days prior to the report. The graduate students we spoke with did not find this an onerous imposition. Several had made such submissions and did not find that it interfered with their publication or presentation schedules. In one instance a post-doctoral researcher slightly modified an oral presentation on TMRI's suggestion in order to avoid divulging the company's proprietary information.

For the graduate students we interviewed, the Novartis Agreement appeared to be a matter of relatively low salience. They did not view it as something that had substantially shaped the environment within their department, nor do they think it has significantly impacted their relationship to students in CNR or in the wider campus community. They do not notice any systematic difference between the research projects funded by Novartis money and those funded by other sources. With respect to the concerns about the Agreement pushing PMB toward more applied-type research, one graduate student told us that of the three laboratories within which she has worked the one using Novartis funds was conducting the least applied and most basic research.

Graduate students appear to have had very limited interaction with industry scientists at TMRI. Since each laboratory only sends two people to the annual "Novartis-PMB Retreat"—usually a faculty member and a postdoctoral fellow—graduate students have rarely participated. Information provided by PMB indicates that only 4 graduate students have attended the first three such retreats, compared to 36 postdoctoral fellows.

The older students, those already enrolled in PMB in 1998, were initially skeptical of the Agreement; a skepticism born largely out of a sense of having been excluded from the negotiation process and having been bombarded by rumors about the profound impact the Agreement would have on their future graduate education.[28] But these students say that once they were able to see the Agreement "in operation" their concerns were largely alleviated. Their view of the consequences of the Agreement is, for the most part, strongly positive. Two things are stressed. First, they are appreciative of the increased financial resources that were made available for the support of graduate students. Second, they consider the opportunity to become conversant with the field of genomics and to utilize the TMRI genomics facility to be a significant benefit. In this way, in their view, the Agreement had assisted PMB in improving its graduate training. Where the graduate students we spoke with

[28] Our findings with respect to PMB graduate student views about the Agreement are consistent with the findings of an opinion survey conducted in early 2000 by Anne MacLachlan of the Center for the Study of Higher Education. See, MacLachlan, "Impact of the Novartis Agreement on Graduate Students in the Plant Microbial Biology Department," Center for the Study of Higher Education, UC Berkeley, July 2000.

expressed reservations, these are in regard to the public controversy that has surrounded the Agreement. Although they consider most of the criticisms of the Agreement to be off-base, they do not like the fact that by virtue of being graduate students in PMB they find themselves in the eye of a political storm. They feel that the Agreement has exposed them to ideologically motivated criticism and unfair stereotyping as "tools of industry." One interviewee told us that in order to avoid being forced to defend herself against criticism she rarely identifies herself to "outsiders" as a student in PMB. Another told us that his dissertation research was set back a year because his experimental plants were destroyed by what he believes were activists opposed to the Agreement.

New graduate students appear to have only the faintest idea about the Novartis Agreement, indicating that it is not a major matter of discussion within PMB. One student did not know anything about the agreement until well into her first year. Another knew about it and the controversies surrounding it prior to enrollment but had heard little since his arrival on campus. It would appear that the department has not made much of an effort to communicate to its graduate students either information about the Agreement's terms or about its operation. Without implying any strong disquiet, the graduate students we spoke with would have liked to hear more from the department about the Agreement and how it is working.

Concluding Observations

The Novartis Agreement was initiated in a veritable storm of controversy. Commentators from within and without the University raised the specter of significant adverse institutional consequences for the Department of Plant and Molecular Biology as well as for the Berkeley campus generally. This review has found that in practice the Novartis agreement has been quite different than what these critical commentaries expected. Indeed, virtually none of the anticipated adverse institutional consequences has been in evidence. The Novartis Corporation and its successor, Syngenta, have assumed a "hands-off" posture with respect to the research conducted by PMB faculty, post-doctoral fellows, and graduate students. The industry representatives on the Novartis program's Advisory and Research committees have not attempted to steer PMB research in any particular direction. They have been willing to support the research projects proposed by departmental faculty, in the same manner as the departmental and campus representatives on these committees. We are aware of no instance in which the industrial "collaborator" sought to target its funding to particular research questions, or in any other way attempted to influence the research direction of PMB laboratories. Nor has the Novartis Corporation, or its successor, blocked the publication of research results emanating from PMB laboratories.

There has been no noticeable movement in PMB's research agenda toward "applied research," as was widely anticipated. Rather, there is a marked continuity with respect to the basic subjects of PMB's scientific inquiries, while a movement to

incorporate the latest advances in genomics and bioinformatics into those inquiries has been facilitated by the Agreement. According to the PMB faculty, the availability of five years of almost certain Novartis funding has allowed them to pursue more novel and innovative lines of inquiry then would have been possible had they had to rely on the usual sources of extramural research funding. At the same time, PMB faculty members have continued to supplement their Novartis funds with extramural research support from other sources. The Novartis program constitutes a significantly smaller proportion of PMB's total research funding today than was the case at the outset of the collaborative relationship (approximately 27% in 2001-2002 compared to 73% in 1997-1998).

The Agreement's stipulation that all PMB participating researchers present abstracts of their papers to Novartis thirty days prior to submission for publication has been honored, but researches do not think that the practice has had any significant impact on the date of actual publication. PMB faculty members have increased somewhat the pace of their publishing since the Agreement's initiation, but the large number of patent filings by Novartis, which some anticipated, has not materialized. Since it takes considerable time for an idea to be reduced to practice, a prelude to making a patent application, there could well be an increase in patent filing activity in the last year of the Agreement.

The Novartis Agreement has had a significant impact on graduate student recruitment. With the funds the Agreement made available for graduate fellowships, PMB has been able to stay competitive with respect to recruiting the very best graduate student prospects. This fellowship money has been used to support first and second year graduate students. It is not targeted to students with any particular research interest, as some anticipated it might be. Indeed, the funds generated by the Agreement are intermixed with other fellowship support money so that there is no identification of a particular fellowship or its recipient with Novartis. Beyond the effect on resources available for graduate student support, the Agreement has not significantly altered the nature of graduate or undergraduate education within PMB. Faculty members teach the same number of courses as before the Agreement's inception, and the curriculum has remained in tact, with the notable addition of several courses in genomics and in microbial biology. The involvement of scientists from Novartis in the supervision of graduate students, anticipated by some, did not materialize.

Given the positive benefits that have accrued to PMB, it is no surprise that the department faculty would wish to continue the existing arrangement into the future. Whether it does, and the reasons if it does not, lie with Syngenta, and thus are beyond the scope of this review.

Our review of the Novartis Agreement has found that it has brought considerable benefit to the Department of Plant and Microbial Biology, and with few, if any, countervailing costs. There has, however, been a considerable indirect cost for the campus—the negative publicity that greeted the Agreement and has, to some extent

persisted. That this publicity has been based, for the most part, on misunderstandings, misperceptions, and erroneous predictions, does not gainsay the fact that most media and public comment on the Agreement has cast the University in an unfavorable light. This situation poses a difficult general policy dilemma for the campus. Should extramural support that furthers the research and teaching mission of the University be eschewed because the source of that support may produce erroneously based critical public comment and negative publicity? An affirmative answer to this question appears unacceptable, since it would permit unintentional misinformation and intentional disinformation to govern University decisions. Instead, what is indicated is an improved effort at presenting an accurate picture to the public of our research and teaching endeavors, and their relationship to extramural funding. At the same time, we need to recognize that some areas of inquiry may be so intermeshed with emotional and/or ideological issues that positive results from such a public education effort may, inevitably, be limited. The Novartis Agreement, enmeshed as it is in the highly contentious and emotional political struggle over genetically modified food ("frankenfood") may present just such a situation.