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Neutron Therapy "Treatment Of Choice" In Salivary Gland Tumors--100 Percent Complete Responses

Preliminary results of a randomized trial comparing neutron and photon radiotherapy for patients with inoperable salivary gland tumors show that neutron therapy is "clearly

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In Brief

FDA Approves Two Alpha Interferons; Canellos To Give Schwartz Lecture At Scripps Meeting

INTERFERON developments have been flowing from federal agencies: FDA last week approved two versions of recombinant alpha interferon for marketing, both for hairy cell leukemia. Schering-Plough's "Intron A", produced under license from Biogen, and Hoffman-La Roche's "Roferon-A", produced in collaboration with Genentech, cleared the final FDA hurdle. The two products, with slightly different genetic origins, have been tested separately and competitively, with similar results. Testing will continue with other malignancies. Meanwhile, Tritus, a joint venture between Triton Biosciences and Cetus Corp., has received the first US patent covering genetically engineered beta interferon, which they have named "Betaseron." It is in phase 2 trials for melanoma, hairy cell leukemia, superficial bladder cancer and rhinovirus. It has also shown results with renal cell cancer, Kaposi's sarcoma, hepatitis B and other diseases. Biogen also announced that it has received a patent for its gamma interferon for treatment of rheumatoid arthritis in West Germany. . . . **ANOTHER NEW** product from the biotech industry is "Novacyte," which its developer, Xsirius Medical Inc. of Rolling Hills Estates, CA, says "is capable of detecting abnormal tissue in the lungs years before it becomes cancerous." The Novacyte test involves sputum cytology and was approved last February by FDA as a prescription device. Suggested price is $120. . . . **T.C. HSU**, chief of cellular genetics at M.D. Anderson, received the Senior Geneticist Award from the Texas Genetics Society at its annual meeting in Houston. . . . **GEORGE CANELLOS**, chief of the Div. of Medical Oncology at Dana-Farber, will present the Bernard Lee Schwartz Memorial Lecture at the 10th annual Scripps Memorial Hospital Cancer Symposium in San Diego Oct. 27. The popular annual update for clinical oncologists will be held in conjunction with the Cancer Symposium for Nurses Oct. 27-29.

Neutron Therapy Called Treatment Of Choice For Salivary Gland Tumors

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the treatment of choice," Thomas Griffin, chairman of the radiation oncology department at the Univ. of Washington, told the Div. of Cancer Treatment Board of Scientific Counselors.

Patients receiving neutron therapy have demonstrated a 100 percent complete response rate to therapy, compared with only 50 percent for those receiving photon therapy, he said. The difference in local control rates is even greater, with patients in the neutron therapy group demonstrating an 88 percent rate of local control compared to only 7 percent for those receiving photon therapy. The preliminary results confirm a retrospective analysis of 102 patients treated in the U.S. and Europe, which found an overall local control rate of 71 percent for patients treated with neutron therapy. That analysis, which incorporated widely varying treatments, found a local control rate averaging less than 40 percent for patients treated with photon therapy, he said. Griffin is chairman of the Neutron Therapy Collaborative Working Group.

Composed of all institutions engaged in NCI supported neutron therapy clinical trials, the group evaluates all previous neutron work in clinical trials and the development of new phase 3 protocols. It also reviews the progress of all protocols. The Radiation Therapy Oncology Group manages the patient data and is responsible for quality assurance and control.

Phase 3 protocols have been designed for carcinomas of the head and neck, prostate, cervix, lung, rectal cancer and tumors of radio-resistant histologies. A protocol is currently under development for inoperable soft tissue sarcoma.

In order to conduct the six phase 3 studies, the group will need a total of 390 patients per year, 195 of whom will have to be treated with neutrons alone, he reported. While acknowledging that the number is ambitious, Griffin said "I think we can do it" because of the participating institutions's accrual history and the addition of two other institutions to the collaborative trials. UCLA's neutron facility is expected to begin patient treatments on its machine June 17. In addition, the Clatterbridge Hospital near Liverpool, England, has agreed to join the multi-institutional cooperative neutron research effort with its high energy, isocentric, hospital based Scanditronix cyclotron.

The Univ. of Washington is collaborating with the Clatterbridge facility by exchanging technologists to assure that patients are treated in an identical manner. Dosimetric intercomparisons between the two facilities are largely complete and the cooperative research effort is expected to begin soon.

As of April 1, the three U.S. institutions participating in the neutron studies had accrued a total of 349 patients on the current contract. The Univ. of Washington has treated the largest number of patients, 236, 212 on the current contract. The Cleveland Clinic Foundation has treated 72 patients on the current contract, and M.D. Anderson has treated 65. Washington's Scanditronix system was ready for the first patient treatment in October 1984. M.D. Anderson, which had signed a contract with the Cyclotron Corp. that declared bankruptcy and went out of business, did not have its system operational until May 1985 and began use of the treatment room in July 1985. UCLA had also signed a contract with Cyclotron Corp. and like, M.D. Anderson, was forced to complete the system itself.

Acknowledging that patient accrual has been the major problem for the Cleveland Clinic, Frank Thomas, chairman of its Radiation Therapy Dept., told the board that the facility "has lagged behind the other contractors." In 1985 and 1986, however, "we have managed to place more patients on study," he said, adding that the board "will see further improvements in patient accrual." The clinic is forming a consortium in order to increase patient accrual, and is reviving a network of area physicians as well as embarking on a physician education campaign to increase the patient pool, he said.

DCT Director Bruce Chabner asked the presenters about efforts to obtain third party reimbursement for neutron therapy. "It's feasible from our side," Griffin replied, adding that all third party carriers have agreed to reimbursement. The university is having problems, however, coordinating state rules with federal rules, he said. M.D. Anderson also has approval from third party insurance carriers, Lester Peters, professor and head of radiation oncology, said. He said that he doubted the hospital will be able to collect on about half of the patients treated because 40 percent of the hospital's

patients are nonpayers and an agreement with the Veterans Administration provides no payment for the therapy.

Board member Robert Goodman cautioned the board that "it would be a mistake for institutions and NCI to try overtly to treat patients who are insured." Chabner replied that NCI will probably ask for collection when possible.

Goodman also stated his support for the program, saying, "In retrospect, the problem was that NCI was paying out major dollars in 1979 when we didn't expect it would take so many years to be operational."

Noting that patient accrual was another significant problem, Chabner told the board that the new contracts will provide a base payment for maintenance of the facilities, with the other 50 percent graded on the basis of controls that will provide an incentive to accrue patients.

Patterns of Care Study in Radiation Therapy Approved By DCT Counselors

NCI's Div. of Cancer Treatment Board of Scientific Counselors has unanimously approved a concept for a four year patterns of care study in radiation therapy. Proposed funding for the competitive award is $600,000 per year.

The concept was prepared as a project to be supported through a contract, through a competitive RFP. The NCI Executive Committee is considering using a grant or cooperative agreement, however.

The project has three main objectives: first, to conduct a new patterns of care study in radiation therapy and to extend the analysis to new tumor sites; second, to conduct a patterns of fractionation study; and third, to conduct a patterns of treatment planning study.

Previous patterns of care studies funded by NCI resulted in important information in the treatment of carcinomas of the cervix, prostate and larynx and in Hodgkin's disease. According to the concept statement, recent studies have identified additional sites where failure analysis might achieve similar useful results. These sites include carcinomas of the prostate, bladder, lung, breast, pancreas, ovary and endometrium and CNS tumors. While board members questioned the inclusion of specific sites, they passed the concept with the inclusion of a recommendation by board member Robert Goodman that DCT seek advice on the process and outcomes related to specific sites. The study will provide "a very innovative way for the specialty to not only police itself, but to evolve what the correct pattern of care is," Goodman said. "For the number of dollars in, it has a direct payout."

Although the original patterns of care in radiation therapy study was funded by the former Div. of Cancer Control, the board appeared to agree with member Karen Fu who said, "This is directly related to cancer treatment, and this [DCT] is where it belongs."

The concept statement says the program will analyze failure patterns in those tumor sites for which data are lacking; develop composite indexes of therapeutic ratio in which relative probabilities of tumor control and late effects are balanced to seek optimal treatments; determine prognostic variables for long term (beyond median) survival, with and without tumor complications; establish a data base for the chronological development of late effects of treatment and exploration of statistical methods that permit best estimates of risk at any point after treatment; and explore new methods of comparison in phase 3 randomized trials.

The program will also assess the outcome of different patterns of fractionated radiotherapy in two leading institutions that employ widely different dose fractionation strategies but reported similar outcomes for specific sites.

Conducted by a radiotherapist, a statistician, and a physicist, the survey will include analysis of therapy and treatment planning records and patient examinations. In addition, the program will determine the extent to which the following are used in radiotherapy treatment planning: CT scanning; MRI scanning; x-ray simulation; two and three dimensional treatment planning; pixel by pixel dose calculations; design of blocks and shields; objective evaluation of rival treatment plans; error analysis; and treatment verification. The study will also assess the use of immobilization techniques and in vivo dosimetry.

The most important aspect of patterns of care analysis is its ability to suggest new approaches to therapy that might improve treatment outcomes, the concept statement says. If local recurrence is the major problem, new approaches to treatment such as radiosensitizers, heavy particles, immuno-

logic delivery mechanisms, new fractionation schemes, or combined modality therapy might be considered. If local control is assured but patients develop distant dissemination, systemic approaches deserve evaluation.

Improvements in conventional radiation therapy may be obtained from altered fractionation schemes. Conventional fractionation patterns for radiotherapy in the U.S. consist of regimens using 1.8-2 Gy/day, five days per week. Experimental evidence, both from the clinic and the laboratory, suggests that better results may be obtained by reducing the dose per fraction and shortening the overall time, and therefore, the average interval between dose fractions.

Shortening the overall treatment time reduces the extent of repopulation by tumor clonogens, although at the risk of compromising reoxygenation. While animal research and ultimately prospective clinical trials will be needed to clearly establish whether the therapeutic ratio can be improved through altered strategies of dose fractionation, accumulation of clinical experience exists in which a spectrum of different dose fractionation schemes have been used. On site surveys are needed because variations in factors such as staging of disease, followup patterns, evaluation of complications, and treatment methodologies, make intercomparisons very difficult. NCI states that "it is widely accepted that improved treatment planning techniques have had a significant impact on the management of certain tumors using radiotherapy." However, there has been no systematic study of the practice of treatment planning. The results of this study will identify areas where present treatment may be improved and will aid in the design of new treatment protocols.

DCT Board To Study "Modification" Of Present Cooperative Group System

NCI executives apparently are willing to settle for modification of the existing clinical cooperative group system rather than one of the more drastic alternatives suggested by the Div. of Cancer Treatment's Cancer Therapy Evaluation Program. The nature and extent of the "modification" might well include some of the features of the CTEP proposals, however, features which would have considerable impact on how the groups operate.

The DCT Board of Scientific Counselors, after listening to DCT staff members, three cooperative group chairmen and a former DCT board member discuss the reorganization proposals, followed the suggestion of their former colleague, Sydney Salmon, that no changes be made before a thorough review by the board of the problems and alternatives.

The board's only action on the matter was to approve a motion referring it to a committee to be named by Chairman Samuel Wells. The committee will report on the board's October meeting, but DCT Director Bruce Chabner said that probably would be too soon for final recommendations and would be only a progress report.

The committee will be chaired by Lawrence Einhorn, professor of medicine at Indiana Univ. Other board members on the committee are Rodrigue Mortel, chairman of obstetrics and gynecology at Pennsylvania State-Hershey Medical Center; Karen Fu, professor of radiation oncology at Univ. of California (San Francisco); and oncoming board member Emil (Tom) Frie, director of the Dana-Farber Caner Institute. Other members are Paul Carbone, director of the Univ. of Wisconsin Clinical Cancer Research Center and chairman of the Eastern Cooperative Oncology Group; Charles Coltman, medical director of the Cancer Therapy and Research Foundation of South Texas and chairman of the Southwest Oncology Group; Charles Balch, director of surgical oncology at M.D. Anderson Hospital & Tumor Institute; Robert Capizzi, director of the Bowman Gray Oncology Research Center and chairman of the Piedmont Oncology Assn.; and Salmon, director of the Arizona Cancer Research Center. CTEP staff members will also serve on the committee.

Salmon led off discussion at the recent board meeting with a review of the last reorganization of the cooperative groups, in 1979-1980. Salmon chaired the board committee then which studied the issues and drew up a list of recommendations that were approved by the board and implemented, for the most part, by DCT. Those included changing the funding mechanism for clinical trials (except for phase 1 and 2 studies) from grants and contracts to cooperative agreements; reducing the size of groups; limiting the number of groups with which institutions and individuals could affiliate; encouraging establishment of regional groups; and more effective coordination efforts by CTEP staff.

The Salmon committee had also recommended that NIH establish a new study section to

review RO1 grant applications in clinical research. An ad hoc study section was formed on a trial basis, but was not found workable, at least to NIH's satisfaction, and a permanent group was never chartered.

Salmon noted that while new regional groups were established, they did not fare well in the last round of review and only one such group--North Central Cancer Treatment Group--still survives. "The regional group concept essentially has been replaced by CCOPs (Community Clinical Oncology Program)," Salmon observed.

"There is no argument, that the 1979 review resulted in some good changes," Chabner remarked. "The question now is, 'Are there changes we can make to deal with the budget problems?' Science has changed since 1979. There was no competition then for funding patient trials with biological therapy. There was no intent in 1979 to freeze the program for the next 10 years."

Michael Friedman, chief of CTEP's Clinical Investigations Branch, described results of the survey of DCT supported clinical research and problems it found (previously reported in the April 11 and subsequent issues of **The Cancer Letter**).Noting that there are two perspectives on the reorganization issue, Friedman said the first is, "If it ain't broke, don't fix it, and the second is, if it ain't fixed, it will break us."

Inflexibility of the Budget

John Killen, CTEP staff member, described some of the budget problems. In the 1985 fiscal year, of the $50.7 million for cooperative groups, $41 million was required for noncompeting groups, leaving just $9.8 million for the seven competing groups. Those groups requested a total of $15.6 million, and 21 miscelaneous requests totaled $2.6 million. The Clinical Cancer Investigation Review Committee recommended $13.8 million, so the competing groups had to be funded at only 85% of the recommended levels. None of the miscelaneous requests were approved, "but we used creative but legal ways to stretch the dollars," Killen said.

The situation is worse this year (FY '86). The original budget for the groups totaled $49 million, with $41.1 million for the noncompeting groups. Gramm-Rudman-Hollings knocked out $1 million of the total, and the need to initiate clinical trials of the LAK-IL-2 therapy took up another $1 million. The 10 competing groups requested $27 million, and 23 miscelaneous requests sought $4.6 million. Noncompeting grants were negotiated down by $2 million, funded at 95% of the previously negotiated amounts. The two successful groups of those recompeted this year, the Pediatrict Oncology Group and Quality Assurance and Review Center, were funded at 93% and 100% of recommended budgets, respectively.

"There is an obvious need now for a urological oncology group," Killen said. "There are other important opportunities, but where will we get the money?"

CTEP Director Robert Wittes said that responses to the various options CTEP had suggested have been coming in since the two meetings he had held with group chairmen and others involved in clinical trials earlier this spring. "The reaction has been cautiously positive on strategy committees and priorty setting, with some significant reservations," he said. "First, no one wanted legislation on what to do. Second, most felt the strategy committees should only cover major phase 3 issues, although there was no unanimity on anything. Third, it was strongly felt that clinical trials groups and centers should be represented on strategy committees.

"We agree that strategy committees should be based in the groups, with ad hoc representation," Wittes said.

On the flexibility of membership issue (one solution for which proposed by CTEP was to permit groups to recruit institutions and physicians for specific studies), Wittes said there was considerable worry about how long term followup could be carried out, that it would lead to destructive competition, and carried with it too many administrative problems. "We no longer think our original proposal is valid," Wittes said. However, one part of that proposal, that one group could participate in a protocol of another, did gain considerable support and should be considered, he said.

"There was a strong feeling against abolishing institutional grants," Wittes continued. "Per case reimbursement is okay, if it is superimposed over institutional grants. Perhaps some institutions could be supported by grants, some by per case."

On the overall structure, "the majority favor retaining the existing system, with some modifications. A minority felt that it was important for surgeons to participate

more. There was no significant interest in a regional group system.

"We are worried about our ability to create new groups as needs arise," Wittes concluded.

When the group chairmen were given the floor, Carbone said that Wittes "has given a fair presentation of the problems. . . One overriding factor to keep in mind is that the science is being done at the major institutions. Academic institutions have to be involved in priority setting. Defense and maintenance of peer reviewed grants is very important."

Also, Carbone continued, "Cooperative groups are a resource for all of NCI, not just DCT" and should be used where appropriate in prevention and control trials. "Groups are not being paid adequately for what they are doing."

Coltman praised Wittes and his staff "for an incredibly comprehensive review of cooperative groups in a thorough way. I think we have come to some consensus."

Coltman suggested that there is flexibility in at least some groups to permit rapid response to changing needs. He cited SWOG's response to the LAK-IL-2 initiative, in which five institution members reacted to the initiative last December, two started accruing patients in April and a third soon will join them. "It is clear we can respond to initiatives," he said. "There is flexibility, and we can move forward."

George Lewis, chairman of the Gynecologic Oncology Group, agreed with CTEP about problems in funding the more productive members. "At times, we have been unable to fund excellent producers. I would like to have a system to permit shifting money where it does the most good. I am concerned about priorities coming from above. I'm concerned about quality. I agree that per case payment and institutional grants would work okay."

Board member Lawremce Einhorn saw things from a somewhat different perspective. "Groucho Marx said he's been rich and he's been poor, and rich is better. At Indiana Univ., we've been in and out of cooperative groups. There are obvious faults in the groups, but they've done a damn good job, over all. Among the benefits have been cancer education, and patients have been placed on protocols when they wouldn't have been without the groups. Intergroup studies have been taking place, and that is a healthy trend. If I were looking at cooperative group problems for the future, I would be concerned about the cost of very expensive technology. I think the LAK cell trials will be a success, but where is the money coming from?"

Einhorn had some doubts about why eight of 10 groups lost their funding this year. "I don't think they did worse in 1985-86 than they did previously, but the budget is worse. I think peer review is taking a hard look at the groups. If we continue with this budget constriction, the groups coming up for renewal in 1988 and 1989 will be facing peer reviewers who are protecting their own funds."

Einhorn is a member of the Southeastern Cancer Study Group, one of those disapproved by the CCIRC. He said that SEG could continue with money from private sources. In fact, he said SEG was already getting three times as much from the pharmaceutical industry as it was from NCI.

"You should be disabused of the notion that the disapprovals had anything to do with budget constraints," Wittes responded. "The rate of escalation in group budgets is such that it will be up to $70 million in the next few years, with or without those groups. There will be no financial relief through the disapprovals. Escalation is built into the out years of grants, and the tendency is always to ask for more at renewal."

On industry funding, Chabner said, "To simply keep alive doing drug company studies is not the reason for cooperative groups' existence, If that is what you want, OK."

"There is no difference in the science for phase 2 studies, "Einhorn said. "Is there any reason why they can't do that (with pharmaceutical industry support)?"

Wittes noted that NCI, the groups and industry representatives had worked out a mechanism to accept industry funds.

Salmon pointed out that the present budget problems could be a drop in the bucket if the LAK-IL-2 trials confirm Steven Rosenberg's results. That treatment is so expensive they could create "a budget disaster," Salmon said. "It could only be solved by Congress."

Einhorn, who developed the regimen incorporating platinum into the drug combination which has placed testicular cancer on the list of those that can be cured, said "In 1974, cisplatin responses were not this good in preliminary results. Nine out of 10 is incredible." Rosenberg had reported LAK-IL-2 responses in nine of 10 renal cell cancer patients treated by NCI so far.

Nurse Shortage At Clinical Center May Be Helped By NIH Policy Change

More than 40 percent of NCI's allocation of beds at the NIH Clinical Center have been closed by the shortage of nurses, a problem created in part by the refusal of NIH leadership to allow NCI to hire nurses into the PHS commissioned corps.

Div. of Cancer Treatment Director Bruce Chabner told his Board of Scientific Counselors that the situation was a "crisis" and that NCI might have to give up intramural clinical research if it was not corrected.

A few days later, NCI Director Vincent DeVita won an agreement from NIH Director James Wyngaarden that will permit the recruitment of nurses into the commissioned corps. That may not entirely solve the problem, but DeVita and Chabner believe it will be of significant assistance.

Chabner said that the NIH entry level for nurses is $2-3,000 a year less than that in the Washington DC area private sector. DeVita said the take home pay for entry level commissioned corps nurses is $800 more per month than the NIH starting salary.

Responding to questions from board members on the reason for NIH opposition, DeVita and Chabner said they had the impression from discussions with Joseph (Ed) Rall, NIH deputy director for intramural research, that NIH is not all that interested in clinical research. "Rall believes beds are something people sleep in when they're not in their labs," DeVita cracked. "Ever since I've been at NIH, there has been this debate of categorical vs. noncategorical research. It's an argument that just takes on different shapes."

The board agreed to a suggestion by member Paul Calabresi that a resolution should be drafted supporting NCI's position. Chabner added that the board's review of the intramural Medicine Branch, for which the NCI nurses work, has given it high marks for the quality of science and importance of its work.

Whatever the argument, it prevailed. DeVita and Philip Amoruso, NCI associate director for administrative management, met with Wyngaarden last week. The NIH director agreed that NCI could start offering nurses the prospect of joining the corps. The advantages: starting salary of $20-21,000 including various allowances; total, free, medical and dental care; military commisary privileges; noncontributory retirement identical to that of the Armed Forces, starting at 20 years with maximum benefits at 30 years service.

NCI is authorized 204 nurses, and there presently are 35 vacancies.

Part of the problem in retaining oncology nurses, Chabner said, is that they "feel they are not really part of the research team. We've tried hard to overcome that. Jan Feldman (new head of Clinical Center Nursing) is out to change that."

Feldman had been acting chief of cancer nursing; Kathy McKeon was appointed to that position when Feldman moved up.

Pinkel, Sharp, Hausen Win 1986 General Motors Cancer Awards

The General Motors Cancer Research Foundation announced the three winners of its $100,000 awards this week:

*Donald Pinkel, who played a major role in developing the first cure for childhood leukemia and contributed significantly to curative chemotherapy for other childhood cancer, won the Charles F. Kettering Prize for excellence in the treatment of cancer. Pinkel was medical director of St. Jude Children's Research Hospital when he led the development of the first effective treatment for acute lymphocytic leukemia. The treatment now cures more than 50 percent of ALL patients. Pinkel is now chief of pediatric leukemia at M.D. Anderson Hospital & Tumor Institute.

*Phillip Sharp, who discovered that genes of higher organisms contain extra parts, called nonsense segments, which do not pass along hereditary information, a finding with important implications for understanding the genetics of cancer, won the Alfred P. Sloan Prize for achievements in basic cancer science. Sharp is director of the center for cancer research at Massachusetts Institute of Technology. His work has contibuted to understanding how cancer genes are switched on and off and how the genes of higher organisms continuously edit the genetic information they are about to use.

*Harald zu Hausen, who discovered the virus that is a major factor in the development of cervical cancer, won the Charles S. Mott Prize for research in cancer causation and prevention. His work in linking human papilloma viruses to cervical cancer and more recently, some cancers of the lungs, larynx, mouth and anus, has been cited as one of the

most important advances in understanding what causes cancer and which may ultimately lead to a vaccine against human HPB.

Each winner will receive a specially minted gold medal, a $100,000 prize, and an additional $30,000 to cover expenses for a scientific workshop or conference.

Pinkel was responsible for developing the concept of total therapy for ALL. His treatment plan included four distinct phases, with different combinations of anticancer drugs used for initial and long term therapy. He showed the importance of specific therapy to the central nervous system in combatting the disease, using radiation therapy alone and in combination with drugs injected directly into the spinal fluid. Margaret Sullivan, professor of pediatrics at M.D. Anderson, has since demonstrated that spinal fluid chemotherapy by itself is as effective as radiation had been.

One of Pinkel's major and most controversial concepts centered on halting the chemotherapy that kept patients in remission. He felt that if they were still in remission after two or three years of chemotherapy, further maintenance therapy was not necessary. He waited until his first seven pediatric leukemia patients had been treated, taken off therapy and followed for five more years before publishing the results. Five of that group continue in good health, one drowned on a fishing trip and the other lived 14 years before dying of another disease.

Hatch Introduces Bill Modifying Delaney Amendment In FDC Act

Sen. Orrin Hatch (R.-UT) introduced a bill this week to "fine tune" the Delaney clauses which exclude from the marketplace any food additive which is found to be carcinogenic in animals or man.

The bill, the "Food Safety Modernization Act of 1986," will give the Food & Drug Administration "additional flexibility in regulatory and review functions, and define the term 'safe' as used in the Food, Drug and Cosmetic Act," Hatch said.

Hatch said he supports the basic intent of the Delaney clauses, which date back nearly 30 years, but "then it was prudent to prevent a product from being used as an additive because even the most minute quantities of harmful substances that could be measured were perhaps still large enough to pose a substantial safety risk. Now, our analytical capacity has advanced so greatly we can measure the presence of carcinogens in parts per trillion, and in some cases can detect individual molecules. This ability has prompted a consensus in the scientific community that many animal laboratory tests at high dosages may have no public health significance and may not necessarily mean significant risks to humans."

Hatch said he drew on recommendations from the scientific and medical communities to define the term "safe" as "a reasonable certainty that the risks of injury to the public health of a substance under the intended conditions of use are negligible." The secretary of the Dept. of Health & Human Services would have the authority to determine what conditions are "neglible".

Hatch said the bill would "allow FDA to focus its scarce resources on substances posing an actual, significant public health threat, rather than expending its efforts on risks which are more theoretical or speculative than real."

The bill would also establish authority for scientific peer review boards that would report to the HHS secretary on scientific questions bearing on additive regulations.

Cosponsors of the measure are Sens. Daniel Inouye (D.-HI), Don Nickles (R.-OK), Steve Symms (R.-ID), Sam Nunn (D.-GA), Ernest Hollings (D.-SC), David Pryor (D.-AR), Tom Harkin (D.-IA) and Howell Heflin (D.-AL).

Consumer advocates have resisted any changes in the Delaney amendment in the past, arguing that carcinogenic thresholds have never been established and therefore it is not unreasonable to ban them totally. The controversy became intense when saccharin was found to cause cancer in some tests, forcing FDA to ban it from the market. Public pressure forced Congress to enact legislation requiring FDA to ignore Delaney in that case.

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