NAS enters human life bill debate

At recent Senate hearings, advocates of the so-called "human life bill" sought scientific validation for their controversial measure. But last week, the National Academy of Sciences, considered the honor roll of U.S. scientists, firmly declined that responsibility, declaring that the bill deals "with a question to which science can provide no answer."

At issue is legislation introduced by Sen. Jesse A. Helms (R-N.C.) that seeks to define human life as starting from conception. If passed, the bill would challenge the 1973 Supreme Court ruling that a woman has a constitutional right to end a pregnancy if she has her doctor's consent. In making that decision, the Court refused to rule on when life begins. Anti-abortion forces feel that if Congress provides that definition, it would give the unborn constitutional rights under the 14th amendment and permit states to pass laws to protect fetuses from the moment of conception. In effect, the bill would allow states to declare abortion murder. Women who have abortions and physicians who perform them would be subject to criminal prosecution.

Science has been drawn into the fray by a statement in Section 1 of the bill that says "present day scientific evidence indicates a significant likelihood that actual human life exists from conception." At hearings held April 23 and 24 before the Senate Judiciary subcommittee on separation of powers, which is chaired by Sen. John East (R-N.C.), a troop of scientists was marched in to testify on that statement. The hearings proceeded amid demonstrations by abortion advocates and accusations that the witness list was stacked in favor of anti-abortionists.

On the first day, all five witnesses told the subcommittee that life begins at conception. According to Micheline M. Mathews-Roth of the Harvard Medical School, "In biology and in medicine, it is an accepted fact that the life of any individual organism reproducing by sexual reproduction begins at conception," which she defined as the "time when the egg cell from the female and the sperm cell from the male join to form a single new cell, the zygote." That conception marks the beginning of human life "is no longer a matter of taste or of opinion," said Pierre Lejeune, French researcher and discoverer of the extra chromosome 21 that marks Down's syndrome, "... it is plain experimental evidence."

Only one witness chose to venture beyond the scientific facts. While agreeing that "the beginning of a human life from a biological point of view is at the time of conception," Watson Bowes Jr. of the University of Colorado School of Medicine cautioned that "it raises very serious issues and problems regarding birth and pregnancy control, induced abortion and the medical care of women .... This straightforward biological fact should not be distorted to serve sociological, political or economic goals."

The second day of hearings broke the scientific unanimity. "I know of no scientific evidence which bears on the question of when actual human life exists," said Leon E. Rosenberg of the Yale University School of Medicine. "I believe that the notion embodied in the phrase 'actual human life' is not a scientific one, but rather a religious, metaphysical one." While the fertilized egg, or zygote, has the potential for human life, he said, science cannot determine when that potential becomes actual. "I maintain that concepts such as humanness are beyond the purview of science because no idea about them can be tested experimentally." Moreover, he added, the bill would prohibit use of contraceptives such as intrauterine devices (IUD's) because they prevent implantation of the fertilized egg, and would halt amniocentesis, the removal of amniotic fluid to test for genetic disorders, because of the small risk of miscarriage. Even the surgical removal from the uterus of a potentially malignant cluster of cells called a hydatid mole would be prohibited, he said, because it is actually a fertilized human egg gone awry.

The statement of the National Academy of Sciences, approved unanimously at the Academy's annual meeting April 28, agrees with Rosenberg's stand. Says NAS president Philip Handler, "We can't improve on [Rosenberg's] statement. The rest of us should stay quiet and let that statement say it." The resolution also faults the proposed bill for using the term "person" to include all human life, saying that "has no basis within our scientific understanding." The crucial statement in Section 1 of the bill "cannot stand up to the scrutiny of science," according to the 100-odd word resolution. "This statement purports to derive its conclusions from science, but it deals with a question to which science can provide no answer....Defining the time at which the developing embryo becomes a 'person' must remain a matter of moral or religious values."

According to Handler, the resolution will be formally transmitted to Congress by an Academy member who will be named to testify at future hearings on the bill. □

NCI finds Laetrile ineffective

Laetrile has failed on four counts: It does not make cancer regress, it does not extend the lifespan of cancer patients, it does not improve cancer patients' symptoms and it does not help cancer patients gain weight or become more physically active. These are the results of clinical tests undertaken in July 1980 by the National Cancer Institute, in conjunction with four major U. S. medical centers—the Mayo Clinic in Rochester, Minn., the University of California at Los Angeles, the University of Arizona Health Sciences Center in Tucson and the Memorial Sloan-Kettering Cancer Center in New York City. The bulk of the results were presented last week in Washington at the annual meeting of the American Society of Clinical Oncology by Charles Moertel, who conducted the Laetrile trial at the Mayo Clinic.

The Laetrile trial included 178 patients with a variety of cancers for whom no effective treatments were available. One-third, in fact, had already received chemotherapy, but it had improved neither their condition nor their survival rate. The patients were given Laetrile for 21 consecutive days by intravenous injection and then orally for an indefinite period or until they showed extremely progressive cancer or died from their cancer. Although a variety of Laetrile regimens have been used by Laetrile advocates, Moertel says, the regimen used in this trial was the same as that currently being employed by Laetrile therapists in Mexico. What's more, patients were treated with a so-called "metabolic therapy" program. The program emphasized a diet of fresh fruits, fresh vegetables and whole grain foods, severely restricted intake of meat, animal products, refined flour, refined sugar and alcohol and included vitamins and minerals.

Results available from the trial to date are based on 156 patients out of the original 178. Of the remaining 22, one was considered ineligible because the initial diagnosis of cancer was not confirmed; two died within three days of starting the treatment from causes not directly related to cancer; one left the study after only eight days and was not evaluable; four patients are still being evaluated; 14 were recently placed on very high doses of Laetrile, and only preliminary data are available for them.

Within one month after starting Laetrile treatment, 50 percent of the 156 patients showed evidence of cancer progression, and 90 percent of them had experienced cancer progression within three months. (This experience, Moertel and his colleagues indicate, would be consistent with that expected if patients had received no treatment.) Only one patient showed any reduction in tumor size. He had metastasizing cancer of the stomach and was first given Laetrile at the Mayo Clinic, then at the University of Arizona. For the first 10 weeks, a tumor that had spread into his neck regressed. But after that the tumor got larger and larger although the patient remained on Laetrile therapy. (A tumor regression rate of zero to five percent is generally expected in studies of inactive

drugs, Moertel and his colleagues explain. In this study, the regression rate represented less than one percent of patients in the study.)

Regarding survival, 50 percent of the 156 patients died before five months, and only 20 percent were alive by eight months. (This survival experience, Moertel and his co-workers report, would be consistent with that expected if patients had received no treatment.)

Of the 156 patients, 140 had had symptoms of their cancer before Laetrile therapy, and of these 140, 19 percent claimed improvement in how they felt at some time during the study. At 10 weeks, only five percent of the patients were still on therapy and claiming improvement in symptoms. (This degree of benefit, Moertel and his team explain, is within the range of that anticipated with a placebo.)

As for weight gain and improvement in physical activity, only six percent of the 156 patients showed weight gain or improvement in physical activity at some time during the study, and only three percent were still on therapy and maintaining weight gain or improvement in physical activity at 10 weeks.

Of the 14 patients recently placed on very high doses of Laetrile, 10 have already shown progressive cancer.

Thus, Laetrile is "ineffective as a treatment for cancer," Moertel and his colleagues conclude.

At a press conference held in conjunction with the ASCO meeting, Moertel said that as the federal government and states make decisions regarding Laetrile use, he hopes they will consider the results of this trial. He also added that he hopes the results will influence cancer patients who are in doubt about whether they should seek Laetrile treatment or not, since "we have tried very hard to conduct a scientifically honest trial." In fact, a corollary study conducted by Karen Redding and co-workers at the University of Arizona on the attitudes of patients getting Laetrile in the trial, compared with the attitudes of cancer patients getting other investigational drugs, suggests that the results of the NCI trial *will* influence cancer patients' decisions regarding treatment. The reason is that patients getting Laetrile showed no significant difference from the other patients in their attitudes toward health, the medical profession, chemotherapy or unproved methods of cancer treatment. Where they differed was in the fact that their physicians had told them that nothing could be done for them.

For persons who adhere to Laetrile in spite of scientifically conducted trials, though, it is unlikely that the NCI trial results will influence their stance on Laetrile in any way. A good example can be found in a Laetrile advocate who popped up in the Laetrile trial press conference and, her voice edged with hysteria, declared, "I'm heartbroken with the results, Dr. Moertel." □

Forbidden fruit of chemical reactions

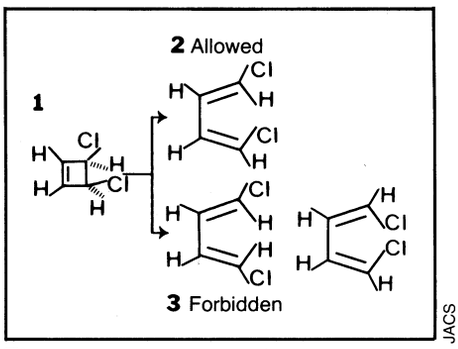
The molecules in a chemical reaction are a fairly predictable bunch. Because of this predictability, chemists depend on a set of laws that explain why molecules A and B will react to form C. Now, Robert M. Moriarty of the University of Illinois in Chicago and colleagues say they have broken one of those laws.

The law they have violated, the Hoffmann-Woodward rule, is one of the newest on the chemical books. For a long time, chemists relied on only two laws to predict the outcome of reactions: steric (two things cannot occupy the same space at the same time) and electric (like charges repel). But there was a need for "some other explanation for some reactions that couldn't be understood by these two sort of classical ways of explaining organic reactivities," Moriarty says, and the Hoffmann-Woodward rule was born.

The Hoffmann-Woodward decree pays attention to where the electrons fit on the complex energy picture of molecules in concerted, or one-step, reactions. Simply put, these electrons occupy certain energy levels called orbitals. According to the Hoffmann-Woodward rule, the conservation of orbital symmetry (a mathematical rather than a physical symmetry) can be used to predict the results of reactions. On the basis of orbital symmetry, therefore, there are allowed and forbidden reaction products. Moriarty and colleagues say they have synthesized such forbidden products in a way that violates the Hoffmann-Woodward rule.

In the April 22 JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, Moriarty and co-workers report zapping *cis*-3,4-dichlorocyclobutene (labeled "1" in the diagram) with the heat energy from a pulsed CO_2 (infrared) laser to open that molecule's ring. This resulted in Hoffmann-Woodward defined forbidden products (3), rather than the expected allowed product (2). To understand the mechanism involved, Moriarty says to think of the electrons in a chemical reaction as crossing a mountain. These electrons will travel the easiest route, the mountain pass, to reach the end of the reaction. Normally, adding more thermal energy will cause these electrons merely to travel more quickly. But, says Moriarty, "We hit the molecule with so much [heat] energy that the electrons shoot up the side of the path" to reach a "forbidden" destination.

Although Hoffmann-Woodward defined forbidden products have been synthesized before, they always resulted from light, not heat, excitation. (In this case, the electrons still are traveling on a pass, but they are crossing "a mountain in the sky," above the "ground state mountain," Moriarty explains.) Producing thermally forbidden products has implications for research on difficult syntheses. For example, thermal



The top structures are isomers — compounds with identical components but different arrangement of them. Lower right compounds (3) are "forbidden isomers."

excitation may be useful for molecular systems unexcitable by light. But, says Moriarty, "I hasten to add that at this stage, it's mainly a theoretical interest that you can [thermally] divert the reaction to a non-allowed pathway."

Moriarty's claim that he can thermally divert the reaction to a non-allowed pathway has met with some criticism in the chemistry community. In fact, he says, "We had a tough time getting it published." Reviewers of his work suggested, for example, that the forbidden products were synthesized via an intermediate product that formed on the walls of the experimental vessel. In such a case, the reaction is not concerted, and the Hoffmann-Woodward rules do not apply. The reviewers also suggested that the forbidden products resulted not from electrons traveling the sides of an energy path, but rather from a rearrangement of an initially formed allowed product. Says Moriarty, "A variety of tests were carried out to eliminate [those] possible artifacts in our experiments." □

Culturing cancer cells

A cancer patient's particular cancer cells can now be grown in the laboratory within 10 days to two weeks, Sydney Salmon of the University of Arizona Cancer Center in Tucson reported in Washington last week at the annual meeting of the American Association for Cancer Research. These cultured cells can be used to test which drugs are most effective. This is important because cancer cells differ from person to person, and a drug that works for one patient may not work for another. In advanced cancer of the ovaries, one of the first cancers to which the method has been applied, Salmon has quadrupled patient survival time.

Salmon uses special nutrients to encourage the growth of cancer cells. In similar work, Israel Vlodavsky and Zvi Fuks of the Hadassah-Hebrew University Medical Center in Jerusalem culture cancer cells on a plastic matrix. □