UNIV - Govt Pat Policy.

McCLELLAN REVERSES HIMSELF, NOW SEES VALUE TO PRIVATE PATENT INCENTIVE ON DRUGS DISCOVERED WITH GOVT. FUNDS; HE FACES POLITICAL REALITIES AND POTENT TESTIMONY

Senate patents subcmte. chairman McClellan (D-Ark.) turned sharply last week from his previous position that the govt. should retain full patent rights on health discoveries touched by govt. R&D money. Instead, he proferred a policy that would offer incentives to drug firms taking heavy financial risks in developing new products.

The Senator's latest turn was executed during a wind-up session of his subcmte.'s hearings on a govt.-wide patent or "exclusivity" policy in connection with discoveries touched by govt. R&D funds. The new look emerged early in the latest and last round, indicating that McClellan may be even more impressed with the political picture in his subcmte.'s parent Judiciary Cmte. than with the potent testimony in what amounted to a "private exclusivity" round for the subcmte.'s hearings.

Conservative Sen. Eastland (D-Miss.) is chairman of the Judiciary Cmte. Ranking Minority member is Sen. Dirksen (R-Ill.). During Senate floor consideration of govt.-take-all patent amendments advanced by Sen. Long (D-La.), a majority of the members of the Judiciary Cmte. lined up against the Louisianan ("The Pink Sheet," July 26).

- Natl. Institutes of Health Director Dr. James A. Shannon provided the biggest "shock factor" during the McClellan subcmte. hearings by candidly opposing the H-E-W Dept.'s govt.-take-all policy.
- SKF President Walter Munns backed up Shannon's statements as to the risk of private investment by providing specific facts and figures from his company's experience. The testimony of a group of university administrators dovetailed neatly with that of Shannon and Munns.
- In another "surprise" development during the hearings, the Senate's "loner" Morse (D-Ore.) spoke out for private exclusivity -- while keeping his liberal skirts clean by repeating Sen. Long's charges against Miles Labs.

SKF PRESIDENT WALTER MUNNS (left) and Dr. Kapp Clark, SKF VP for R&D, give Senate Patents subcmte. facts and figures on risks of private investment in developing new drug products.

"In the field of medicine," McClellan told the wind-up session, "there's got to be an incentive somewhere to get somebody to put up the risk captial." Only last month (July 6) McClellan had observed during hearings: "If the federal govt. goes out here and provides money to universities and institutions and laboratories to develop a product to benefit the health of the people of the nation, that is an area where I think the govt. might very well take the patent and let the product be available to all mfrs."

In concluding the hearings McClellan all but ruled out the possibility of coming out with a patent bill this session. Noting that 100 specific amendments were offered

8/23/65 Copies of pages 24-29 for Ross, Wm. Young, Woerpel, Bremer, Poston, Kesse, Abrams.

to four pending bills and that 800 pages of printed testimony had been taken, he said: "I have no desire to delay action on this subject. But if judicious consideration is to be given, suggestions carefully weighed and evaluated, and if sound legislation is to be brought out, it will obviously be necessary that lengthy and careful study be given of this record. How long it will take the subcmte. to mark up a bill I wouldn't even try to guess." He also announced the hearing record would remain open to Aug. 31 to permit inclusion of additional statements if any are forthcoming.

> The H-E-W Dept. had sought during its testimony on alternative bills pending before McClellan's subcmte. a delay in any legislative enactment. The dept. can and does take title to any discoveries touched by govt. funds, and its ultimate objective -- govt. title, period, in the health field -- could be served no better by any legislation.
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> NIH Director Shannon bluntly set forth his misgivings over the H-E-W govt.-take-all patent policy and said NIH top brass have felt that as persons responsible for the largest federal medical research program "there does need to be clarification of the situation with regard to the issuance of licenses to inventions held by the govt."

One possible escape from this dilemma, he suggested, would be to grant short periods of exclusivity where it is found necessary to develop an invention to the point of practical application and there is no other way to obtain the needed industry cooperation.

According to Shannon, compounds which show some promise in early stages of investigation may be of no benefit to the public and may not serve the public interest unless clinical testing is undertaken and the resulting drug is cleared by FDA and marketed.

It's In The Public Interest To Encourage Support Of Research From Industry, Shannon Says

"We also believe that it seems sensible to be able to involve industry in the testing and marketing phases of drug development since these firms already possess capabilities in these areas that would have to be duplicated elsewhere to accomplish these necessary purposes," he explained.

Shannon said NIH support of an investigator may stop at an early stage of development or cover only a part of the complicated sequence of drug development. Regardless, he said, NIH patent policy requires that his invention in most instances is complete within the definition of the U. S. Patent Office. He continued that the PHS Surgeon General's disposition generally results in title to the govt. in accordance with provisions of H-E-W regulations, the title provisions of the President's Memorandum (on patents) and an Executive Order governing disposition of employee inventions.

"The uncertainties involved in after-the-fact determination have created barriers for collaboration by the drug industry with NIH-supported scientists in bringing potential therapeutic agents to the point of practical application," Shannon testified, continuing:

> "The industrial firms want some guarantee of exclusive patent rights as compensation for and protection of their possible investment, which may be considerable before FDA clearance can be obtained. Because, as I understand it, there is some question as to whether we can or should extend such a guarantee, it is often difficult to motivate industry to undertake the perfection and marketing of the NIH-supported inventions."

Shannon said one of the common characteristics of scientific research activities performed in universities is receipt of joint and simultaneous support from govt. and non-profit organizations and not infrequently from industry. (more)

Where the private sources of support impose no conditions upon their grant relating to inventions the H-E-W regulations requirement that NIH grantees report all their inventions to the Surgeon General for his disposition poses no problem, he explained.

On the other hand, Shannon said, the Amer. Cancer Society and the Amer. Heart Assn., maintain patent policies requiring grantees to agree to assign all invention rights to them. The grantee who accepts support for the same research activity from both NIH and sponsors like these has undertaken conflicting obligations he cannot fulfill, Shannon noted.

"It is difficult to solve problems of conflict after the fact on the basis of priority as between the co-sponsors," he told the subcmte. "Neither is it a satisfactory solution to suggest that the grantee be limited to acceptance of support from only a single source which imposes such an obligation."

The witness said he believes it's in the public interest to encourage support of research from the private sector of the economy and to discourage exclusive reliance upon govt.-financing. To which he added: "In order to further this objective, it may be necessary to relieve universities and their researchers from the dilemma created by conflicting obligations to assign patent rights."

Shannon said it's his understanding that H-E-W patent regulations at this time do not take into consideration the equities of co-sponsors in making disposition of inventions arising from research financed by multiple sources "and the Surgeon General must make his determination solely on the basis of our support." These regulations, he pointed out, have been under review for some time by the dept.

SKF President Munns Offers Three Principles In Determining New Patent Legislation

Questioned sharply on some of these points by McClellan, the NIH director noted, "There should be some way of balancing equities -- some realistic assessment of the equities." While stating that he would not suggest that a product whose development was financed by the govt. be given to a private firm for "full exploitation," he insisted drug firms must have some incentive if their cooperation in such work is to be obtained in a competitive economy.

McClellan seemed concerned with the high degree of risk experienced by drug firms in producing new products. Dr. Shannon produced these figures: Less than one out of ten drugs survive between initial discovery and marketing,and the one that does costs these companies from $200,000 to $400,000 to develop. "If I were industry I would not take that risk," Shannon said.

McClellan put it another way, "If the govt. goes so far and no further and the govt. says it will take the patents -- who will accept the risks?" Shannon replied, "No organization will take that risk."

He said some form of license exclusivity would pave the way for negotiations between govt. and industry and this could lead the way to marketing a new drug discovery.
McClellan: "There should be some incentive for somebody to take this risk."
Shannon: "I fully agree."

McClellan at this point reiterated his own uncertainty of what can be done to resolve the patent question. Addressing his comments to Shannon, the Senator said: "Unless the govt. wants to take over the whole thing -- and you're not equipped to do it -- there should be a way of licensing it. How to develop a statute, a procedure, to do this, to assure them some protection -- this is a very difficult area. How to find an equitable solution is the problem."

Walter A. Munns, president of Smith Kline & French Labs., offered a set of three principles which he urged the subcmte. to consider in determining the form of any new patent legislation involving inventions touched by federal support. These principles:

- Where a scientist working in a non-profit institution and supported by govt. funds discovers a new compound that may have medicinal use, the patent rights should belong to his institution, subject to certain govt.-retained controls.

- The non-profit institution should have the right to negotiate with industry to carry out screening, testing and development work, and may further negotiate a royalty-bearing license with industry -- subject again to govt.-retained controls. The license agreement may also define the respective rights of the non-profit institutions and the industrial concern as to new uses and related development and improvements which may result from collaborative work between them.

- In view of the substantial expenses which must be borne by the industrial concern to develop and test the compound -- and considering that the royalties will accrue to the institution and be available for further research (with such reward to the individual inventor as the institution deems appropriate) -- the license to the concern must be attractive enough to invite its participation in this research and development.

Munns illustrated the "tremendous gulf" that exists -- in terms of time, research effort and money -- between a new and patentable chemical compound and a safe and effective medicine in a bottle that can be used to treat human beings.

He cited as an example the last product introduced by SKF -- a new diuretic discovered by the firm and marketed in 1964. The generic name of the compound is triameterene and it was marketed under the trademark "Dyrenium."

Munns Says Cost Of Developing Dyrenium Couldn't Have Been Justified Sans Patent Exclusivity

Munns said the expense of the patentable invention probably did not exceed $50,000. But to transform triameterene into a marketable item cost SKF 5-1/2 years effort and more than $2 mil. of its own funds.

SKF'S DEVELOPMENT COSTS FOR DYRENIUM

ACTIVITY	MONTHS	COST TO SK&F
1. From beginning of animal tests to decision to test in man	15	$ 350,000
2. From beginning of clinical testing to New Drug Application submission	18	735,000
3. From New Drug Application to Food and Drug Administration approval	33	1,014,000
GRAND TOTAL	5 yrs./ 6 mos.	$2,099,000

"This was a hazardous speculation," he testified. "At any time during this process the product might have been shown to have some property that would have made it unsuitable for human administration, and our work and expenses to that date would

have gone for nothing. We could never have justified this speculation without the exclusivity provided by a patent."

Munns gave another illustration which he said shows the complications that arise under present patent policy. Again, he cited an SKF experience. In 1958, he explained, his company began working with a university scientist who had been studying certain steroids for several years under a PHS grant of $26,000 a year.

Then, as today, SKF had a program in the field of atherosclerosis and heart disease and was determining the effect of compounds on blood cholesterol. This effect was not one of these specifically under investigation by the university in question, nor was it contemplated in the PHS grant. Munns said SKF was able to demonstrate that the compound lowers the cholesterol level of blood without the side effects which, in the past, have limited other drugs used for this purpose.

"We are now at the point where it should be given to humans for preliminary evaluation," Munns told the subcmte. "But to date we have been unable to conclude an agreement that will give use reasonable exclusive rights, even though our investment in development already amounts to approximately $250,000 and may well amount to a couple of million dollars before the compound becomes a medicine for human use. We are continuing to negotiate."

Sen. Morse (D-Ore.) urged the subcmte. to come up with a bill containing a clear policy statement that "taxpayer-financed R&D property is a natural resource belonging to the people of the United States and must be safeguarded accordingly."

Although Coming Out For Private Exclusivity, Morse Burnishes Liberal Image Via Long.

But Morse recommended offering exclusive licenses for three to five years, subject to renewal if the contractor shows he is making an effort to develop a patent.

Although coming out for private "exclusivity," Morse burnished his "liberal" image by picking up for repetition the charges repeatedly asserted by Sen. Long that Miles Labs overcharged for a PKU test kit developed by U. of Buffalo researcher Dr. Robert Guthrie with govt. funds. Sen. Long has pressed for govt. legislation that would allow private rights only in extremely exceptional cases.

While title to the Guthrie invention was in the hands of the govt., Morse asserted, commercial mfrs. were producing a PKU test for 1-1/2¢ to 2¢ per baby, and making a profit. However, when Miles claimed a patent on the test, it was priced at $.52 per baby.

Another witness, Maurice H. Seevers, chairman of the U. of Michigan medical school's dept. of pharmacology, warned that unless some degree of exclusivity is granted to an inventor, cooperation between industry, academic institutions and govt. -- "so vitally necessary to any successful program in such a high-risk area as drug development" -- will not be forthcoming.

He told the subcmte. he sensed "a rising and accelerating tide of discontent among university scientists relating to excessive governmental control of pharmaceuticals and other chemicals." And this, he added, "is manifest primarily as a strain on university-industry and indirectly on university-govt. relations, which have flourished so well in the past in developmental drug research."

Lewis Nobles, dean of the U. of Mississippi graduate school -- Judiciary cmte. chairman Eastland's home state -- recommended that most patent rights arising from

PHS grants to universities should be released by PHS, with reasonable safeguards, to the universities. If desirable, he said, a period of market exclusivity would be negotiated by the university with a commercial company and royalties would be paid to the university. In every instance, however, the govt. would obtain a non-exclusive, royalty-free license for its use.

C. M. Suter, director of Sterling-Winthrop Research Institute, Rensselaer, NY, opposed a recently-instituted NIH policy which permits biologists to determine whether compounds made under NIH grants have a potential for practical value. He said this policy is set forth in a section of the McClellan patent bill and "has largely blocked collaboration between scientists of universities and other non-profit research groups and the pharmacologists in industrial labs.

"The industrial people cannot logically invest in this effort because all results which might lead to a useful product are subject to confiscation by the NIH without recompense," Suter testified.

Joseph B. Sprowls, dean of Temple U. school of pharmacy, testified he is in favor of legislation "which is neither discriminatory nor confiscatory and which permits an equitable arrangement for patent ownership with institutions which have made major contributions to patentable discoveries."

Edward F. McKie, testifying for the Amer. Bar Assn., supported a recently introduced patent bill of Sen. Dirksen (R-Ill.). He agreed with the bill "that the govt. should never be permitted to take the exclusive right to an invention for the purpose of excluding its citizens from the practice of that invention."

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COURT CASE THAT COULD BE A LANDMARK FOR FDA IN MAKING JUDGMENTS ON SUSTAINED RELEASE PRODUCTS EXPECTED TO BE DECIDED IN SEVERAL MONTHS

A case that could become a landmark for the Food & Drug Administration (FDA) in making judgments on sustained release products is expected to be decided in two or three months. If the govt. wins, the decision could give FDA medics legal boundaries for medical decisions in the following areas:

- sustained release drugs' benefits-to-risk ratio;
- how rapidly a long-acting drug can act to correct a condition without being administered in toxic dosages;
- whether release is in an even, consistent pattern;
- the difficulty of eliminating a sustained release drug from the patient's tissues should a toxic condition develop.

The recent court action in Federal District Court in St. Louis stemmed from seizure in December 1964 of Wynn Pharmacal's Quinaglute Dura-Tabs, a sustained release form of quinidine gluconate, indicated for use in cardiac arrhythmias.

The court decision could influence FDA's Kefauver-Harris efficacy evaluation of sustained release products marketed before the new law. Drugs in sustained release dosage form are seventh on an agency effectiveness review list.

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