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STATEMENT OF DR. CHARLES L. FOX, JR., M.D.
PROFESSOR OF SURGERY AND MICROBIOLOGY
COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS & SURGEONS
NEW YORK, NEW YORK

AT THE JOINT PRESS CONFERENCE OF
SENATOR ROBERT DOLE OF KANSAS
AND
SENATOR BIRCH BAYH OF INDIANA

ANNOUNCING

THE INTRODUCTION OF A BILL ESTABLISHING A FEDERAL PATENT POLICY
FOR UNIVERSITIES AND SMALL BUSINESSES TO DEVELOP
INVENTIONS FUNDED WITH GOVERNMENT SUPPORT

CONFERENCE HELD IN ROOM 318 RUSSELL SENATE OFFICE BUILDING
WASHINGTON, D. C.

AT 9:30 A.M.
WEDNESDAY, 13 SEPTEMBER 1978

STATEMENT OF DR. CHARLES L. FOX, JR., M.D.

I AM CHARLES L. FOX, JR., M.D., PROFESSOR OF SURGERY AND MICROBIOLOGY, AT COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS & SURGEONS, NEW YORK, NEW YORK. I AM GRATEFUL FOR THE OPPORTUNITY TO BE WITH YOU TODAY. I AM THE INVENTOR OF SILVER SULFADIAZINE, A LIFE-SAVING AGENT FOR THE TREATMENT OF BURNS. I AM HERE TO TELL YOU OF THE IMPORTANCE OF SILVER SULFADIAZINE, HOW IT WAS DEVELOPED, SUPPORTED, AND FINALLY MADE AVAILABLE TO BURNED PATIENTS IN HOSPITALS AND AT MILITARY INSTALLATIONS.

FIRST, I WOULD LIKE TO TELL YOU A LITTLE SOMETHING ABOUT BURNS. PRIOR TO AN UNDERSTANDING OF THE PROBLEM OF BURN SHOCK IN THE MID-1930'S, MOST PATIENTS SUFFERING BURNS GREATER THAN 40% OF THE TOTAL BODY SURFACE DIED OF BURN SHOCK WITHIN 36 HOURS OF THE INJURY. WITH THE RECOGNITION THAT LARGE AMOUNTS OF FLUIDS WERE NECESSARY TO PREVENT THIS SHOCK IN LARGE AREA BURNS, PATIENTS WITH BURNS OF ALL SIZES BEGAN TO SURVIVE THE EARLY POST-BURN PERIOD. THESE PATIENTS WITH LARGE BURNS WHO SURVIVED THE INITIAL SHOCK PHASE, HOWEVER, WENT ON TO DIE FROM INFECTION IN 10-21 DAYS THE PRIMARY CAUSE OF THIS INFECTION WAS IN THE BURN WOUND ITSELF.

WITH THE ESTABLISHMENT OF BURN WOUND INFECTION AS THE CAUSE OF DEATH IN THESE PATIENTS, METHODS TO CONTROL IT WERE SOUGHT IN THE LATE 50'S AND EARLY 60'S. THE FIRST APPROACH, SYSTEMIC ANTIBIOTICS, WAS FOUND TO BE OF LITTLE VALUE BECAUSE OF THE LACK OF CIRCULATION IN THE BURN WOUND AND THEIR INABILITY TO KILL THE PREDOMINANT BACTERIA. WITH THE FAILURE OF SYSTEMIC ANTIBIOTICS, LOCAL MEASURES WERE SOUGHT TO CONTROL THE SPREAD OF BACTERIA AND THE DEVELOPMENT OF LIFE-THREATENING INFECTION IN THE BURN WOUND.

DURING THE EARLY 1960'S SOME SUCCESS WAS FOUND IN THE USE OF TOPICAL SILVER NITRATE SOLUTION IN A 1/2% CONCENTRATION. AT THE SAME TIME, A SULFA COMPOUND, MAFENIDE, WAS DEVELOPED WHICH WAS ABLE TO HELP CONTROL BURN WOUND INFECTION. IT HAD A HIGH DEGREE OF ACTIVITY AGAINST MANY FORMS OF BACTERIA AND HELPED DECREASE MORTALITY IN MANY BURNS. BOTH OF THESE AGENTS, HOWEVER, HAD SEVERE SIDE EFFECTS WHICH MADE THEM NOT ONLY DIFFICULT TO USE BUT ALSO ADDED TO THE BURDEN OF THE PATIENT IN SOME CASES.

LATER ON IN THE 1960'S, WORKING IN MY LABORATORY AT COLUMBIA UNIVERSITY WITH PARTIAL FUNDING OF SOMEWHAT LESS THAN $100,000 ON THE PART OF NIH, I SYNTHESIZED AND SCREENED MANY MANY COMPOUNDS WHICH MIGHT BE EFFECTIVE IN THIS AREA OF BURN WOUND INFECTION. I FINALLY FOUND SILVER SULFADIAZINE TO BE THE MOST EFFECTIVE IN LABORATORY ANIMALS.

I THEN RECEIVED FROM A COMMERCIAL DRUG COMPANY THE NECESSARY MATERIALS FOR THE EVALUATION OF THIS COMPOUND IN HUMANS AND TO MEET THE MEDICAL NEEDS FOR BURN THERAPY OF THE PATIENT POPULATION IN SOUTH VIETNAM THAT WAS UNDER THE AUSPICES OF THE UNITED STATES STATE DEPARTMENT SURGICAL TEAM TREATMENT FACILITIES. BASED ON THE RESULTS FROM THE CLINICAL USE, IT BECAME APPARENT THAT SILVER SULFADIAZINE COULD POSSIBLY BE THE PRODUCT OF CHOICE FOR TREATING MAJOR BURNS. IT ALSO BECAME CLEAR THAT WE WOULD NEED THE CONTINUING SUPPORT OF PRIVATE ENTERPRISE IN THE FORM OF A REPUTABLE PHARMACEUTICAL MANUFACTURER IN ORDER TO DEVELOP THE OPTIMAL FORMULATION AND TO CONDUCT THE PRECLINICAL AND CLINICAL EVALUATIONS REQUIRED BY THE FOOD AND DRUG ADMINISTRATION. I FELT THAT SILVER SULFA_ DIAZINE COULD PROVIDE THIS COUNTRY WITH A MAJOR BREAKTHROUGH FOR TREATING

BURNED PEOPLE BUT WITH LESS INCIDENCE OF SIDE EFFECTS THAN CURRENTLY AVAILABLE THERAPY.

TO LOCATE A COMPANY TO ACCOMPLISH THESE OBJECTIVES, THE ASSISTANCE OF RESEARCH CORPORATION WAS ENLISTED. RESEARCH CORPORATION'S CONTRIBUTION WAS TWOFOLD. FIRST, THEY RECOGNIZED THAT EXTENSIVE PATENT PROTECTION MUST BE OBTAINED TO JUSTIFY THE SIGNIFICANT EXPENDITURE REQUIRED TO BRING SILVER SULFADIAZINE TO THE POINT WHERE IT COULD BE USED IN LIFE-THREATENING BURN SITUATIONS THROUGHOUT THE UNITED STATES AND, IN FACT, THROUGHOUT THE WORLD. RESEARCH CORPORATION ALSO DEVELOPED A SUCCESSFUL WORKING RELATIONSHIP BETWEEN MYSELF, COLUMBIA UNIVERSITY, THE NIH, AND A QUALIFIED COMPANY FROM THE AMERICAN PHARMACEUTICAL INDUSTRY. MOST MAJOR PHARMACEUTICAL COMPANIES WHO EXPRESSED INITIAL INTEREST HAD SERIOUS DOUBTS REGARDING PATENT VALIDITY, AND THE RESTRICTIONS WHICH WOULD LIKELY BE PLACED ON THEIR MARKETING EXCLUSIVITY TO WARRANT THE EXPENDITURE REQUIRED TO BRING IT TO THE MARKET PLACE AND THE PATIENT'S BEDSIDE.

FINALLY, LICENSING ARRANGEMENTS WERE MADE WITH MARION LABORATORIES OF KANSAS CITY TO DEVELOP, TEST AND SECURE FDA APPROVAL FOR A SUITABLE SILVER SULFADIAZINE TOPICAL PRODUCT. MARION WAS SUCCESSFUL IN DEVELOPING A FORM OF SILVER SULFADIAZINE FOR APPLICATION DIRECTLY TO BURNED PATIENTS.

THIS PRODUCT WAS STUDIED UNDER MARION'S DIRECTION IN 2500 CLINICAL CASES AT ALL MAJOR U.S. BURN CENTERS. FDA APPROVAL FOR MARKETING WAS GRANTED NOVEMBER 26, 1973, APPROXIMATELY FOUR YEARS AFTER THE LICENSE ARRANGEMENT WAS CONCLUDED. AS A CONSEQUENCE, SILVER SULFA DIAZINE IS NOW IN GENERAL USE.

IN SUMMARY, THE DEVELOPMENTS OF SILVER SULFADIAZINE IS AN EXAMPLE OF HOW IMPORTANT AND SOMETIMES LIFE-SAVING PRODUCTS, WHICH HAVE BEEN PARTIALLY FUNDED BY HEW, CAN MAXIMIZE CONTRIBUTION TO PUBLIC WELFARE.

IN PREPARING TO SPEAK TO YOU TODAY, AND AS A DOCTOR INVOLVED IN ALLEVIATING HUMAN SUFFERING AND PAIN, I WAS HAPPY TO LEARN THAT AFTER EXPENDITURE OF OVER 3 BILLION DOLLARS IN NIH GRANTS TO UNIVERSITIES, OF

THE 28,000 PATENTS IN THE PATENT OFFICE PORTFOLIO, "ONE OF THE PETITIONS GRANTED INVOLVED A BURN OINTMENT DISCOVERED AT A UNIVERSITY, WHICH WAS PATENTED FOR THE UNIVERSITY BY RESEARCH CORPORATION, LICENSED TO A PHARMACEUTICAL COMPANY, CLINICALLY TESTED UNDER THE DIRECTION OF THE COMPANY, AND CLEARED BY THE FOOD AND DRUG ADMINISTRATION ON THE COMPANY'S INITIATIVE. THE DRUG IS NOW COMMERCIALLY AVAILABLE. TO MY KNOWLEDGE, THIS IS THE ONLY DRUG OUTSIDE THE CANCER CHEMOTHERAPY PROGRAM WHICH WAS INITIALLY DISCOVERED WITH DEPARTMENT SUPPORT AND HAS REACHED THE MARKET-PLACE THROUGH THE INVESTMENT OF RISK CAPITAL FROM THE DRUG INDUSTRY."