

TUESDAY MORNING 10 DECEMBER 1991

The morning session was convened at 8:00 a.m. with Clayton Fuller serving as moderator.

Taxol Update

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For as long as man has inhabited the earth, his medicine has been derived from plant parts—roots, stems, leaves, flowers and fruits. I do not propose to present an exhaustive list of plants, worldwide, and their remedy, but a few examples: hemlock (powdered), controls headlice; hemlock (chewed), stops bleeding; salmon-berry bark, numbs toothaches; thimbleberry leaves, strengthens blood; and *Artemisia*, anti-malarial. Obviously, the list of plants is endless and many of the world's museums have displays relative to this topic, such as seen in the marvelous museum in Sydney, Australia. Many scientists, including my good friend, Dr. Ed Croom, have spent time with various native people observing the time-honored practice of healing by the use of plant parts. Some of these studies included a monkey searching a specific plant to cure a particular malady. The scientist would then identify the genus/species with the assistance of a competent botanist.

On 17 April 1991 as a part of the I.P.P.S. International Board Pre-Tour, I visited Thursday Plantation, Ballina, New South Wales, Australia. This nursery, founded in 1979, is producing plants of *Melaleuca alternifolia* not for the landscape trade, but for the pharmaceutical market. They market Australian tea tree oil for virtually any body rash or itch known to man! Their annual production is one million seedlings, transplanted to their plantations. Their return from the extracted medicine for 1990 was one million dollars.

In July of this year, many of us read with great interest, the excellent discourse written by fellow member, Peter Del Tredici (Del Tredici, 1991), entitled, "*Ginkgo* and People—A Thousand Years of Interaction". Peter described a 1,000 acre nursery in Sumter, South Carolina, which harvests, dries, bales and ships *Ginkgo* leaves to Europe for extraction. Gross sales in 1988 amounted to about \$500 million. This *Ginkgo* leaf extract has demonstrated a positive effect in increasing vasodilation and peripheral blood-flow rate in the capillaries of patients suffering from a variety of circulatory disfunctions. It has also proven effective in a number of other maladies, including arthritis.

I mentioned the above two examples, *Melaleuca alternifolia* and *Ginkgo*, as a prelude for discussion of another plant genus, *Taxus*. I first heard the word taxol, which is a derivative of taxane, in 1988. In 1989, I initiated R&D project 89-2 for our nursery. Since that date, I have accumulated reams of data. Our sister and brother I.P.P.S. members have been very kind in sending me copies of magazine and newspaper articles relative to this topic. I am very proud to have had comments sent

to me from all six of our I.P.P.S. regions. These contributions to my files range from International President Bunker to our own Paul Smeal, whose most recent communication was two weeks ago.

I propose, at this point, to briefly explain the origin of taxol, where the plant propagator fits into this puzzle today and what my crystal ball sees for the future.

In the mid 1950s, a chance discovery by researchers at Eli Lilly Company, prompted the National Cancer Institute (NCI) to implement a major program to discover anti-cancer substances from natural sources—plants! In the late 1960s, preparations from *Taxus*, especially extracts of *T. brevifolia* bark, were shown to be quite cytotoxic. Then, in 1971, a group at Research Triangle Institute isolated pure taxol. Due to the scarcity of the drug, only a few cancer types have been investigated to date. Nonetheless, excellent response has been demonstrated for advanced refractory ovarian cancer. This result has been verified in more extensive human cancer treatment studies. NCI has announced that the efficacy of taxol in ovarian cancer warrants full clinical development. Once available commercially, it is estimated approximately 10,000 to 12,000 ovarian cancer patients each year would receive treatment, creating a need for roughly 50 pounds of taxol each year—just for the United States. As the potential of taxol to treat other cancer types is realized, and early results in breast cancer are very promising, even greater quantities of the drug will be required to meet the clinical need. At this point, I want to note that the pure taxol produced to date has only been produced from the bark of *T. brevifolia*, not from needles and twigs of a cultivated plant source. This leads us into developments initiated in 1988 and continuing to date.

In October 1989, Ken Cochran, curator of Secrest Arboretum and Ed Croom, Research Institute of Pharmaceutical Science, University of Mississippi, visited with me at Zelenka Nursery, Inc. Due primarily to the efforts of Cochran and Croom, an organization named, The Alliance of Growers and Universities for *Taxus*, was formed.

In November of 1989, I was invited to Washington, D.C. to attend a USDA sponsored meeting. This meeting generated much verbiage, very little positive action and my introduction into bureaucracy! Truly incredible!

In March of 1991 representatives from Rhode Island Nurseries, Studebaker Nurseries and Zelenka Nursery, along with Ken Cochran, met with representatives from the Natural Products Institute, University of Mississippi at the OARDC in Wooster, Ohio. The name of the organization was changed to The Alliance for the Production of Taxol. Among positive actions this meeting generated a letter sent to some 70 plus *Taxus* producers asking them to sign a commitment agreement which, among other things, will inventory *Taxus* species/cultivars by age and availability for potential drug extraction.

The first drying of *Taxus* clippings took place at Zelenka Nursery on 6 April 1991. I hasten to add that the biomass for a potential multi-billion dollar drug is being dried in a 45 year old corn dryer! Sounds incredulous, but it is true. Drying took place through May and early June, 1991, and on 12 June 1991, NCI denied a proposal from the alliance (through USDA) to produce taxol from needles/twigs of *Taxus* cultivars. It is ironic that at about this time the Forest Service was given permission to allow the harvest of 750,000 pounds of bark from *T. brevifolia* for 1991. These 100 year old, plus trees (supposedly the slowest growing conifer in North America) are admired by many environmentalists and also, are the habitat of the spotted owl. It is reported that three to six trees yield enough bark to produce

taxol to treat one lady. The alliance has constantly maintained that the nursery community has a sustainable source of supply with our cultivated *Taxus* plants, rather than the rape of our native western yew.

Zelenka started drying again in September with biomass received from Rhode Island Nurseries, and clippings received from Fairview Nurseries in October. November, December and January drying activities involved whole plants received from Gardner Nursery. Other than a few cultivars for clinical testing, all drying has consisted of *T. x media* 'Hicksii'. On 16 September 1991 Zelenka Nursery received a cooperative agreement from USDA to produce (and dry) 100,000 lb of *T. x media* 'Hicksii' for the cancer treating drug, taxol. The first shipment, after much delay, is scheduled to ship next week. Time will tell!

Now, where does the nursery community, and particularly the plant propagator, fit into the taxol program?

First of all, anyone growing *Taxus* can join the alliance. Your contact is Ken Cochran, Secret Arboretum, who can advise you as to the questionnaire, contract, etc. If I can help, please ask me. Second, is there a potential for a *Taxus* second market, one for drug production? The answer is definitely affirmative! The vast majority of nurseries are more comfortable in supplying biomass from clippings, cull plants, and propagation waste rather than gamble with dedicated acres without a contract. In my view, contracts will be on the horizon, probably offered by someone outside our nursery community. I urge you to carefully review any contract extended to you!

I have celebrated 69 birthdays on this planet and am probably more naive today than I was as a child. I can recall, in 1989, how great this Research and Development project was going to be. First, and foremost, the humanitarian feature of my nursery community saving ladies' lives with normally discarded clippings from pruning, propagation waste and culled plants. We would gather the waste from our *Taxus* plants, send the material off to some magical facility for drying, extraction and purification, and quickly the drug taxol would appear! How naive can one be?

My friends, I have learned that the pharmaceutical industry does not subscribe to our motto of "To seek and share". I don't understand, nor do I adhere to a mentality of confidentiality. This has been very difficult for me, to say the least. I can contact the University of Wisconsin and discuss taxol with Brent McCown or Dave Ellis, who are conducting taxol intercellular research, quite comfortably because we are I.P.P.S. brothers.

I am not allowed to enjoy that type of dialogue with pharmaceutical companies around the world. It is apparent, one view is first, to save lives and the other view is, profit foremost.

The Alliance is viable because most growers in the Alliance have propagators and production people who are I.P.P.S. members. As plant propagators, we once again have the opportunity to utilize the plant parts of *Taxus* to save lives, in addition to beautifying the world. All of us have a tremendous challenge and by seeking and sharing, we definitely will meet and accept and conquer the challenge.

LITERATURE CITED

- Del Tredici, P. 1991. Ginkgo and People: A Thousand Years of Interaction. *Arnoldia* 51(2): 2-15.