A MESSAGE FROM THE PRESIDENT

The 1996/1997 year of the AOCD is in full swing as we reach the halfway mark. The mid-year meeting held in Jackson Hole, Wyoming, chaired by Greg Papadeas, D.O., was a huge success and reaffirmed our standard of high quality. This also marked our first meeting to be accredited by the AAD and the AOA for CME. As always, the logistical support provided by the Kirksville College of Osteopathic Medicine, through Rita Harlow and her staff, augmented the efforts of Becky Mansfield and our central office to truly make this another in our long list of outstanding programs.

Our sights are now turned to the annual meeting held in conjunction with the AOA in San Antonio, Texas. October the 19th-23rd. Chairman Lynn Sikorski, D.O., is planning innovative changes in our program. More information will be coming from Lynn in the very near future.

The new AOCD Speakers Bureau is up and running. We currently have several members who have indicated an interest in being part of the Speakers Bureau. Becky is in the process of notifying the various state societies and other AOA affiliate groups about our Speakers Bureau. Our intent is to increase the presence of the AOCD at these various educational meetings with special emphasis on educating primary care physicians.

There are many new initiatives which came out of the Executive Committee meeting held at Jackson Hole. First and foremost, is the approval of the report of the Bylaws Committee which undertook a massive reorganization of both the AOCD Constitution and the AOCD Bylaws. A listing of the specific changes will be provided to the membership approximately thirty days prior to an annual meeting for evaluation. We intend to bring this to a vote of the entire membership at the annual meeting on October 21.

One of the major changes that have been proposed in the Constitution would revise the criteria for active membership in the AOCD. If this proposal is approved, any member of the AOA who is board certified by either the American Osteopathic Board of Dermatology or the American Board of Dermatology will be eligible to apply for active membership.

The Editorial Committee, under the direction of Dr. Ron Miller, continues to work hard on improving the quality of our publications. Since this is a very formidable task, we continue to need membership input to the Editorial Committee and Dr. Miller.

Two other exciting innovations were presented and passed by the Executive Committee. The first is the establishment of a pilot program which would provide funding for one member of the AOCD to take a fellowship in dermatopathology. The Executive Committee is hoping that this will not only provide an opportunity for one of our members to complete a fellowship, but would also encourage that individual to be an active participant in the future training of our residents.

The Committee also proposed and passed a policy to establish a pilot program to fund a one year fellowship in pediatric dermatology. This policy is intended to increase the expertise within our College in the area of pediatric dermatology and provide still another educational resource for our residents. More information on both of these pilot programs will be forthcoming at the annual meeting in October.

Our national office in Kirksville, continues to pick up the pace as it fulfills the requirements for the development of the new OPTI program. This new mandated AOA program has profound effects on residency training programs, not only in dermatology, but in all AOA post-graduate education. If you are involved in a post-graduate training program, either as a trainer or trainee, you are encouraged to keep in touch with Becky at the central office for the latest developments.

As all of these innovations and developments continue to unfold, the members of your Executive Committee and I, need and look forward to your input. See you in San Antonio!

Fraternally yours,
Edward H. Yob, D.O.
President
Applications for the Speakers Bureau are available through the AOCD Office.

MEMBERSHIP RENEWALS are due JULY 1
Support the AOCD and Renew NOW!

LECTURE:
RONALD C. MILLER, D.O.
"COMMON NEOPLASMS OF THE SKIN"
Generations Rediscovered
Ninth Annual Weekend for Women
February 21 & 22, 1997
CMU’s Bovee University Center
Mt. Pleasant, MI

DERMPATH FELLOWSHIPS
If you are interested in a Dermpath Fellowship contact:
Ms. Naomi Smith
c/o AFIP
Washington D.C. 20306-6000
Phone # 202-782-2148

DR. GENE GRAFF
elected President-Elect of the Washington State Dermatology Association for 1997-98.
In 1998 he will become President.

AAD RECEPTION
sponsored by Medicis
Thursday, July 31, 1997
New York City
Watch for Notice in Mail!
1997 AOCD Scientific Seminar

I would like to take this opportunity to invite each of you to attend the annual convention and scientific seminar of the AOCD, to be held in conjunction with the AOA, October 19-23, 1997, in San Antonio, Texas.

Our college's activities begin with Board and mock Board examinations to be held Sunday, October 19. Also, the Executive Committee Meeting will be held at this time. Sunday evening we will have a welcome reception, which will hopefully capture the spirit and energy of San Antonio.

Didactic sessions begin Monday, October 20. This day will include cosmetic dermatology lectures by Kevin Pinski, M.D., and James Fulton, M.D. There will also be a pediatric dermatology lecture by Adelaide Hebert, M.D. The AOCD Annual Banquet will be the focus of the evening. I will continue with Dr. Yob's precedent of a formal, quality dinner. The evening will continue with a dessert buffet. It should prove to be the perfect opportunity to catch up with your colleagues.

Tuesday's sessions will begin with Dr. Del Rosso's Therapeutic Update. This will include a presentation by our first international speaker, Piet De Doncker, Ph.D... who has been active in the development of the newer antifungals. Also, Charles Camisa, M.D., will do presentations on oral lesions and difficult psoriasis cases. Alex Kowalczyk, M.D. will lecture on pigmented lesions, as well as oversee the Dermatopathology Scholarship presentation. We will also hear from our own Dr. Monique Cohn. Our business luncheon and meeting is scheduled for Tuesday, and in the evening the AOA will have the President's reception and banquet.

Wednesday will begin with a managed care and coding update by the popular Inga Ellzey, who always has practical, and valuable tips. Zoe Draelos will speak on moisturizers. Please set aside some time for the interesting resident presentations as well.

San Antonio provides an atmosphere where everyone can have fun! We will be in close proximity to the famous Riverwalk, the convention center, the Alamo, and numerous shopping areas. The weather should be very comfortable at this time of year. In response to many comments by our members, I will try to resurrect the spouse's event, and develop a program that will appeal to men, women, and children.

Please plan on attending...a great time should be had by all!

Lynn Sikorski, D.O.

---

John Crosby, JD, Named Executive Director of American Osteopathic Association

(Chicago) -- John Crosby, JD, became the executive director of the American Osteopathic Association (AOA) on May 12.

"I am joining the AOA to help launch the second 100 years of this tremendous organization," stated Crosby. "I hope to focus on member services because they are the lifeblood of any voluntary professional group. Given the outstanding staff that I have inherited and the support of the AOA Board of Trustees, I know we will succeed."

He joins the AOA from the American Medical Association (AMA), where he spent six years as senior vice president for health policy and was actively involved with policy development and strategic planning.

---

Thank You

A very special thank you goes to all the AOCD members who offered prayers and support during my mother's illness and death.

You are a caring, compassionate group who have made my job much easier during this time.

Becky Mansfield

---

e-mail

The national office now has a new e-mail address available to anyone on line. Contact us at:
aocd@vax2.rainis.net
1997 Midyear Meeting Highlights

Richard Bennett, M.D.  
Lynn Drake, M.D.  
Mark Dahl, M.D.

KOPRINCE AWARD WINNERS  
Midyear Meeting 1997 • Jackson Hole, Wyoming

DANIEL BUSCAGLIA, D.O.
MARY LOU ERNST, D.O.
JEFFREY G. WEAVER, D.O.

*** CONGRATULATIONS!! ***

Greg Papadacos, D.O.  
Program Chair

Friday morning lecture attendees.

Dr. & Mrs. Roger Byrd (L)  
Dr. Dudley Goetzte (C)  
Dr. & Mrs. Earl Bachenberg (R)  
Relaxing after Friday Night Banquet.

Swing Dancing  
Lessons after the Banquet
Meetings Update

The 1997 AOCD Midyear Meeting, held at the Snow King Resort, in Jackson Hole, Wyoming was a delightful event. The Academic program led by Dr. Gregory Papadeas was excellent. Presentations by members of the College including Dr.'s Conte, Del Rosso, Ziering, and Benedetto, were informative and thought-provoking. We also were privileged to enjoy updates by guest speakers including Dr's. Lynn Drake, Mark Dahl, Richard Bennet, Joseph Eastern, Scott Sulentich and Joseph Morelli.

The social program began on Wednesday with a gala opening reception and extended through a wonderful Friday evening of western Bar-B-Q highlighted with country and western dancing. During the meeting spouses and guests enjoyed the unique little shops, wild life, and historical tours, and ski events provided enjoyment for all. Did anyone buy a Jackalope or have a beer on the saddle at Cowboy's?

Mark your calendars now for the 1998 Midyear Meeting to be held in Williamsburg, Virginia. The dates are Wednesday, April 1, 1998 through Saturday, April 4, 1998. Dr. Jim Young will head the academic program. There will be an opportunity to tour the historic Williamsburg village which depicts and recounts the fascinating hardship and adventure of pre-revolutionary colonial living. The area contains one-of-a-kind buys and many family activities including Busch Gardens. Hope to see you there.

The 1999 Midyear Meeting is currently planned for the Aspen, Colorado area. More information as the plans are finalized will be published in the newsletter. Possibilities are being discussed for the 2000 Midyear Meeting. Locations on the table for discussion include a cruise, Hawaii, or Whistler, Canada. If you have any suggestions, comments, or concerns regarding the midyear meeting sites, please feel free to contact me by fax at 314-831-9301 or call Becky Mansfield at 1-800-449-2623.

Robert F. Schwarze, D.O.
Chairman of Site Committee

Midyear 1997 Exhibitors

Allergan Skin Care
AmeriPath, Inc.
Brymill Cryogenic Systems
Dermatopathology Lab of Central States
Dermik Laboratories, Inc.
Ferndale Laboratories, Inc.
Healthpoint
Huma Tech Laboratories

ICN Pharmaceuticals
Medical Software Management
Medicis - The Dermatology Co.
Oclassen Pharmaceuticals
Ortho Pharmaceutical
Procter & Gamble
Sandoz Pharmaceuticals
Sharpland Lasers

& Steifel Laboratories

Thank You to our 1997 Midyear exhibitors.
We appreciate your support and contributions to our program.
The Corporate Membership Program

The AOCDE Corporate Membership Program was created to allow corporations to play an active role in the education of osteopathic dermatology residents and the ongoing training of practicing osteopathic dermatologists.

The AOCDE administers educational programs on a national level encompassing the very latest in medical and pharmaceutical research. It is only through the generous financial support of our Corporate Members that we are able to attain our goal of providing state-of-the-art education to our physician members.

Our physician members rely on the education and training the AOCDE provides, and recognize the integral role every AOCDE Corporate Member plays in that process.

Categories of Corporate Members are:

DIAMOND CIRCLE CORPORATE MEMBERS
PLATINUM CIRCLE CORPORATE MEMBERS
GOLD CIRCLE CORPORATE MEMBERS
SILVER CIRCLE CORPORATE MEMBERS
& BRONZE CIRCLE CORPORATE MEMBERS

More details on the Corporate Membership Program may be obtained through the AOCDE National Office.

PUBLISHED

DANIEL A BUSCAGLIA, D.O.
EUGENE CONTE, D.O.
WENDY McCAIN, R.N. &
SHELLY FRIEDMAN, D.O. F.A.O.C.D.

"THE TREATMENT OF CELLULITE WITH METHYZANTHINE AND HERBAL EXTRAXT BASED CREAM: AN ULTRASONOGRAPHIC ANALYSIS"

COSMETIC DERMATOLOGY
Vol. 9, No. 11 November 1996

Resident News

Farewell to our residents who finished their training this summer. We wish them success in their future practices:

DANIEL BUSCAGLIA, D.O.
ROBERT FINKELSTEIN, D.O.
KEITH MACKENZIE, D.O.
EUGENE NOWAK, D.O.
BRIAN PORTNOY, D.O.
BRYAN SANDS, D.O.
JOSEPH URASHI, D.O.
JEFFREY WEAVER, D.O.
MARTIN YUNGMANN, D.O.
SHARON ZELLIS, D.O.

Hello to our new residents who are beginning their training:

DANIEL J. ABRAHAM, D.O.
KATHRYN BALEZ, D.O.
DEBRA DALY, D.O.
MARK K. HORENITZ, D.O.
ELIZABETH A. REISINGER, D.O.

ANNUAL REPORT DEADLINES

All annual training report documentation (resident's report, program director's report and scientific paper) is due in the national office 30 days after you complete each year of your training. Incomplete documentation will not be reviewed by the Education Evaluation Committee. Documentation must be received no later than August 18, 1997 for review at the September meeting.

DAVID W. DORTON, D.O.
MARK KAUFMANN, M.D.

"PALMOPLANTAR PUSTULES IN AN INFANT"

ARCHIVES OF DERMATOLOGY
Vol. 132, No. 11 November 1996
CALL FOR APPLICATIONS

CE.R.I.E.S. RESEARCH SUPPORT AWARD
250,000 FF

CE.R.I.E.S.

THE EPIDERMAL AND SENSORY RESEARCH AND INVESTIGATION CENTER (CENTER DE RECHERCHES ET INVESTIGATIONS ÉPIDERMHIQUES ET SENSORIELLES - CE.R.I.E.S.)...

is an autonomous research center based in Paris, France and funded by CHANEL to perform and encourage research on the physiology and biology of healthy skin. In addition to conducting its own independent research, the CE.R.I.E.S. is funding an annual Award.

PHYSIOLOGY OR BIOLOGY OF HEALTHY SKIN AND/OR ITS REACTIONS TO ENVIRONMENTAL FACTORS...

The CE.R.I.E.S. Research Support Award is intended to honor and support a dermatologic researcher with a proven track record in fundamental or clinical research work on the physiology or biology of healthy skin, for a one year period.

The awardee will be selected by an international jury consisting of the members of the Scientific Advisory Board of the CE.R.I.E.S..

The 1996 CE.R.I.E.S. Award went to Dr. Akira Takashima of the University of Texas Southwestern Medical Center for research into the molecular basis for Langerhans cell-specific transcription of the Dectin-1 gene.

DEADLINE FOR APPLICATIONS: JULY 17, 1997

Request for application forms must be addressed to:

CE.R.I.E.S. Research Support Award
c/o CHANEL, 9 West 57th Street, New York 10019
Tel: 212-688-5055 - Fax: 212-752-1851

Award will be granted without regard to sex, age, race, religion, national origin, creed, disability, marital or veterans status.
American Osteopathic College of Dermatology

A SPECIAL THANK YOU
1996-1997
Corporate Members

DIAMOND
AmeriPath
Janssen Pharmaceutica

PLATINUM
C & M Pharmacal, Inc.
Schering Laboratories

GOLD
Dermik Laboratories, Inc.
Fenidale Laboratories, Inc.
Galders Laboratories
Glaxo Dermatology
Medicis Pharmaceutical Corporation
Oclenss Pharmaceutical Corporation
Ortho Pharmaceutical Corporation
Sandoz Pharmaceuticals Corporation
SmithKline Beecham
Westwood Squibb Pharmaceuticals

SILVER
Allergan

BRONZE
Procter and Gamble
Stiefel Laboratories

ASSOCIATE WANTED:

Practice dermatology in a 42 member-multi specialty clinic located in Southern Illinois. There are only three dermatologists serving over 200,000 people in a nine county area. Dermatologists within our service area have a high profile practice with earnings well above the national average. Our clinic is located only 2 hours south east of St. Louis. Please contact Andy Marcce or Sue Ridgay at 800-333-1929 or check out our website @ <www.sih.net/recruit> Sorry, no J-1 opportunities.
It's time for a change in antiviral therapy.

Proven to reduce all symptoms and shorten viral shedding in acute recurrent genital herpes*

Proven to shorten postherpetic neuralgia in acute uncomplicated herpes zoster††

*In clinical studies designed for medication to be administered within 6 hours of symptoms or lesion onset.
† FAMVIR therapy is more effective when started within the first 48 hours of rash onset. There is no information on efficacy when the drug is started more than 72 hours after rash onset.
‡ Measured as median duration; FAMVIR has no effect on the incidence of postherpetic neuralgia.

It's time to choose

HERPES ZOSTER

FAMVIR

famciclovir

RECURRENT GENITAL HERPES

500 mg
3x/day
7 days
125 mg
2x/day
5 days

Advancing antiviral treatment

©SmithKline Beecham, 1997

Please see brief summary of prescribing information on adjacent page.
FAMVIR: Famciclovir Tablets

See complete prescribing information in SmithKline Beecham Pharmaceuticals literature. The following is a brief summary.

INDICATIONS AND USAGE: Famciclovir is indicated for the management of acute herpes zoster infections and for the treatment of recurrent genital herpes.

CONTRAINdications: Famciclovir is contraindicated in patients with known hypersensitivity to the drug.

PRECAUTIONS: Famciclovir has been shown to be effective in patients with moderate-to-severe renal impairment, and no dosage adjustment is necessary.

ADVERSE REACTIONS: In controlled clinical trials, the most common adverse events reported with famciclovir were headache, nausea, diarrhea, and vomiting. The incidence of these adverse events was similar to that observed with placebo. No significant laboratory abnormalities were reported.

Dosage and Administration:

- For the treatment of herpes zoster, the recommended dosage is 125 mg four times daily for 7 days.
- For the treatment of genital herpes, the recommended dosage is 250 mg three times daily for 5 days.

It's time for a change.

FAMVIR: Safety/tolerance

Generally well-tolerated in clinical trials

The most commonly reported adverse events for FAMVIR and placebo, respectively, are headache (zoster: 22.7% vs 17.8%; genital herpes: 23.7% vs 16.4%) and nausea (zoster: 12.5% vs 11.6%; genital herpes: 10% vs 8%).

The efficacy and safety of FAMVIR have not been established in children, uncompromised hosts, patients with herpes zoster complications, patients with first episode genital herpes, or in patients with renal or hepatic insufficiency. All clinical trial populations consisted of otherwise healthy adult populations.

ASSERTIVE REACTIONS

- Herpes Zoster: In four clinical studies involving 818 Herpes zoster patients with herpes zoster (FAMVIR 250 mg four times daily for 5 days), the most frequent adverse events associated with FAMVIR were headache and nausea. The incidence of these adverse events was similar to that observed with placebo.
- Recurrent Genital Herpes: In three placebo-controlled clinical trials involving 528 patients with recurrent genital herpes (FAMVIR 125 mg three times daily for 5 days), the most frequent adverse events associated with FAMVIR were headache and nausea. The incidence of these adverse events was similar to that observed with placebo.

FAMVIR is contraindicated in patients with known hypersensitivity to the drug.

PRECAUTIONS: Famciclovir has been shown to be effective in patients with moderate-to-severe renal impairment, and no dosage adjustment is necessary.

ADVERSE REACTIONS: In controlled clinical trials, the most common adverse events reported with famciclovir were headache, nausea, diarrhea, and vomiting. The incidence of these adverse events was similar to that observed with placebo. No significant laboratory abnormalities were reported.

Dosage and Administration:

- For the treatment of herpes zoster, the recommended dosage is 125 mg four times daily for 7 days.
- For the treatment of genital herpes, the recommended dosage is 250 mg three times daily for 5 days.
LAMISIL® Tablets for onychomycosis
due to dermatophytes (tinea unguium) may represent

A new standard of success in onychomycosis

Nail it!

...with high cure rates, low relapse*

* In toenails (12 weeks of therapy) (N=465)
  In clinical trials, 70% of patients achieved mycological cure, 59% of patients achieved effective
treatment, and 38% of patients demonstrated mycological cure plus clinical cure
  (Mean time to overall success: 10 months), mycological cure is achieved before clinical cure
* 85% of patients who achieved mycological cure plus clinical cure of toenails did not relapse *

...with a clear difference

* No BOX WARNINGS or CONTRAINDICATIONS based on drug-drug interactions
* Compatibility with commonly prescribed medications such as terfenadine (Seldane®), digoxin, warfarin

Lamisil® Tablets
(terbinafine HCl tablets) 250mg

With onychomycosis...

NAIL IT from start to finish

Terbinafine clearance is decreased 33% by cimetidine, 16% by terfenadine (Seldane), and increased 100% by rifampin.
Generally mild and transient side effects.
LAMISIL Tablets is contraindicated in individuals who are hypersensitive to terbinafine.
Rare incidences of symptomatic hepatobiliary dysfunction and isolated cases of serious skin reactions (eg. Stevens-Johnson Syndrome and toxic epidermal necrolysis) have been reported. In such cases, therapy should be discontinued. Please see WARNINGS in brief summary of full prescribing information.

* Price data based on the 10% of patients who demonstrated both mycological cure plus clinical cure
Ricldaxen (terbinafine) Tablets is a registered trademark of Hoechst Marion Roussel, Inc.
Please see brief summary of full prescribing information at the end of this advertisement.
NAIL IT!... With patient satisfaction

- The only short treatment regimen for fingernails
- Once-a-day dosing
- Can be taken with or without food

**Priced lower than Sporanox® capsules:**

* Based on average wholesale price (AWP) of recommended doses. The AWP of a 12-week course of Lamisil® Tablets is about 50% less than the AWP of a 12-week course with inadequate therapy. This comparison is based on prior data. The AWP does not necessarily represent price to pharmacy or patient, or other costs.

**REFERENCES:**
2. Reed BJ. Membran N. Medical economics. 1994;459.

**INDICATIONS AND USAGE:** Lamisil® (terbinafine hydrochloride tablets) Tablets are indicated for the treatment of onychomycosis of the toenail or fingernail due to dermatophytes (tinea unguium) (see DOSAGE AND ADMINISTRATION in the full prescribing information).

**CONTRAINDICATIONS** Lamisil® (terbinafine hydrochloride tablets) Tablets are contraindicated in individuals with hypersensitivity to terbinafine.

**WARNINGS:** Rare cases of symptomatic hepatobiliary dysfunction including cholestatic hepatic hepatitis have been reported. Treatment with Lamisil® (terbinafine hydrochloride tablets) Tablets should be discontinued if hepatobiliary dysfunction develops (see PRECAUTIONS). There have been isolated reports of serious skin reactions (e.g., Stevens-Johnson Syndrome and toxic epidermal necrolysis). If progressive skin rash occurs, treatment with Lamisil® should be discontinued.

**PRECAUTIONS:** General: Changes in the ocular lens and retina have been reported following the use of Lamisil® (terbinafine hydrochloride tablets) Tablets in controlled trials. The clinical significance of these changes is unknown. Hepatic function (hepatic enzyme) tests are recommended in patients administered Lamisil® for more than six weeks (see WARNINGS).

In patients with either pre-existing liver disease or renal impairment (creatinine clearance <50 ml/min), the use of Lamisil® has not been adequately studied, and therefore, is not recommended (see CLINICAL PHARMACOLOGY, Pharmacokinetics in the full prescribing information).

Transient decreases in absolute lymphocyte counts (ANC) have been observed in controlled clinical trials in placebo-controlled trials. 44% Lamisil-treated patients (1.7%) and 31/123 placebo-treated patients (2.2%) had decreases in ANC to below 1000/mm^3 on two or more occasions. The clinical significance of this observation is unknown. However, in patients with known or suspected immunodeficiency, physicians should consider monitoring complete blood counts in individuals using Lamisil® therapy for greater than six weeks. Isolated cases of severe neutropenia have been reported. These were reversible upon discontinuation of Lamisil®, with or without supportive therapy. If clinical signs and symptoms suggestive of secondary infection occur, a complete blood count should be obtained. If the neutrophil count is <1,000/mm^3, Lamisil® should be discontinued and supportive management started.

**Drug Interactions:** In vitro studies with human liver microsomes showed that terbinafine does not inhibit the metabolism of tobutamidine, ethinylestradiol, ethacrynic acid, and cyclosporine. In vivo drug-drug interaction studies conducted in normal volunteer subjects showed that terbinafine does not affect the clearance of antitrypase, digoxin, and the antihistamine terfenadine. Terbinafine does not affect the clearance of warfarin or warfarin's effect on prothrombin time. Terbinafine decreases the clearance of inhaled and/or administered theophylline by 15%. Terbinafine increases the clearance of cyclosporine by 15%.

Terbinafine clearance is increased 100% by ritonavir, a CYP450 enzyme inducer, and decreased 33% by cimetidine, a CYP450 enzyme inhibitor. Terbinafine clearance is decreased 16% by terfenadine. Terbinafine clearance is unaffected by cyclosporine.

There is no information available from prospectively conducted drug interaction studies with the following classes of drugs: oral contraceptives, oral replacement therapies, hypoglycemics, andophyllines, phenothiazines, thiazide diuretics, beta blockers, and calcium channel blockers.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** In a 28-month oral carcinogenesis study in rats, a marginal increase in the incidence of liver tumors was observed in males at the highest dose level, 69 mg/kg/day (11.8 x the maximum recommended human dose (MRHD) based on body weight (BW) and surface area (BSA)). There was no dose-related trend and in the mid-dose male rats (20 mg/kg/day, 4 x the MRHD based on BW and 1 x the MRHD based on BSA) did not have any tumors. No increased incidence in liver tumors was noted in female rats at doses levels up to 30 mg/kg/day (5.4 x the MRHD based on BW and 4.5 x the MRHD based on BSA) or in male or female mice treated orally for 23 months at doses up to 156 mg/kg/day (51.2 x the MRHD based on BW and 3.9 x the MRHD based on BSA).

A wide range of in vivo studies in mice, rats, dogs, and monkeys, and in vitro studies using rat, monkey, and human hepatocytes suggest that terbinafine is not a tumor promoter in liver tumors in the high-dose male rats. May be associated with peroxisome proliferation, and support the conclusion that this is a rat-specific finding. In vivo investigations included evaluations of the effects of Lamisil® on liver weight, morphology, and ultrastructure; hepatic cytochrome P450, and peroxisome proliferation assessed morphologically and biochemically (peroxisome enzymes) in mice, rats, dogs, and monkeys. The effects of Lamisil® and two known metabolites on hepatic morphology and peroxisomal and P450 enzyme activities were also evaluated in vivo in male rats and in vitro in primary hepatocyte cultures from male rats and humans and from monkeys. The results of the in vivo investigations indicated that oral administration of Lamisil® (500 mg/kg/day) resulted in peroxisome proliferation in rats and that these effects did not occur in mice, dogs, or monkeys. Further, in vitro studies indicated that peroxisome proliferation occurred in rat hepatocytes, but not in monkey or human hepatocytes.

Systemic exposure to Lamisil® assessed by the steady-state plasma unbound fraction area under the curve (AUC) for terbinafine and metabolites, was 7.7 and 9.5 mg·h/mL for male and female rats, respectively, and 11.2 and 13.1 mg·h/mL for male and female mice, respectively, at doses comparable to the high doses in the carcinogenicity studies in humans. In humans subjects at the MRHD (a daily dose of 256 mg of Lamisil®), the unbound AUC was 0.466 mg·h/mL. The resulting safety margins for humans, based on relative systemic exposure (AUC unbound), in rats and mice were 1.2 x to 2.4 x 24 to 28, respectively.

The risks of a variety of in vitro and in vivo genotoxicity tests gave no evidence of a mutagenic or clastogenic potential, and demonstrated the absence of tumour-inducing or cell-proliferating activity. Oral reproduction studies in rats at doses up to 300 mg/kg/day (63 x the MRHD based on BW and approximately 12 x the MRHD based on BSA) did not reveal any specific effects on fertility or other reproductive parameters. Intraperitoneal administration of terbinafine hydrochloride at 153 mg/kg in pregnant rabbits did not increase the incidence of abortions or premature deliveries nor affect fetal parameters.

**Pregnancy Category B:** Oral reproduction studies have been performed in rabbits and rats at doses up to 300 mg/kg/day (63 x the MRHD based on BW and approximately 12 x the MRHD based on BSA) and rats, respectively, based on BSA) and have revealed no evidence of impaired fertility or harm to the fetus due to terbinafine. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, and because treatment of onychomycosis can be instituted until after pregnancy is completed, it is recommended that Lamisil® not be initiated during pregnancy.

**Nursing Mothers:** After oral administration, terbinafine is present in breast milk of nursing mothers. The ratio of terbinafine in milk to plasma is 7:1. Treatment with Lamisil® is not recommended in nursing mothers.

**Pediatric Use:** The safety and efficacy of Lamisil® have not been established in pediatric patients.

**ADVERSE REACTIONS:** The most frequently reported adverse events observed in the 3 US-Canadian placebo-controlled trials listed in the table below. The adverse events reported encompass gastrointestinal symptoms (including diarrhea, dyspepsia, and abdominal pain), liver test abnormalities, rashes, urticaria, pruritis, and taste disturbances. In general, the adverse events were mild, transient, and did not lead to discontinuation from study participation.

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Lamisil® (%) n=465</th>
<th>Placebo (%) n=137</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>12.9</td>
<td>9.5</td>
</tr>
<tr>
<td>Gastrointestinal Symptoms</td>
<td>5.6</td>
<td>2.9</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4.3</td>
<td>2.9</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>2.4</td>
<td>1.5</td>
</tr>
<tr>
<td>Nausea</td>
<td>2.6</td>
<td>2.9</td>
</tr>
<tr>
<td>Flatulence</td>
<td>2.2</td>
<td>2.2</td>
</tr>
<tr>
<td>Dermatological Symptoms</td>
<td>6.5</td>
<td>2.2</td>
</tr>
<tr>
<td>Rash</td>
<td>5.6</td>
<td>2.2</td>
</tr>
<tr>
<td>Pruritus</td>
<td>2.8</td>
<td>1.5</td>
</tr>
<tr>
<td>Urticaria</td>
<td>1.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Liver Enzyme Abnormalities*</td>
<td>3.3</td>
<td>1.4</td>
</tr>
<tr>
<td>Taste Disturbance</td>
<td>2.8</td>
<td>0.7</td>
</tr>
<tr>
<td>Visual Disturbance</td>
<td>1.6</td>
<td>0.0</td>
</tr>
</tbody>
</table>

*Liver enzyme abnormalities = upper limit of the normal range.

**Rash** adverse event: Based on worldwide experience with Lamisil® (terbinafine hydrochloride tablets) Tablets, use includes: symptomatic idiopathic hepatobiliary dysfunction (including cholecystic hepatitis) (see WARNINGS and PRECAUTIONS), serious skin reactions (see WARNINGS), severe neutropenia (see WARNINGS), and allergic reactions (including anaphylaxis). Rarely, Lamisil® may cause taste disturbance (including taste loss) which usually resolves within a few weeks after discontinuation of the drug.

Store tablets below 25°C (77°F) in a tight container. Protect from light.

Sandoz Pharmaceuticals Corporation. East Hanover, New Jersey 07936

APRIL 1996

P37051901