

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
21-043

MICROBIOLOGY REVIEW

Consultative Review to OTC
Division of Anti-Infective Drug Products (HFD-520)
Clinical Microbiology Review Notes #1

NDA # 21043

DATE COMPLETED: 29 JAN 1999

APPLICANT(NDA):

Soltec Research USA
48 Mt. Olive Road
Budd Lake, NJ 07828

CHEM/THER. TYPE: Plant extract

SUBMISSION REVIEWED: Original dNDA

PROVIDING FOR: Approval of a pediculocide under an OTC monograph

PRODUCT NAMES(S):

Proprietary: Rid Mousse

Non-Proprietary/USAN: pyrethrum

DOSAGE FORMS(S) Aerosolized mousse for hair

STRENGTHS: 0.33 %

ROUTE(S) OF ADMINISTRATION:

Topical application to hair

PHARMACOLOGICAL CATEGORY:

Antiparasitic

DISPENSED: Rx OTC

INITIAL SUBMISSION:

Received by CDER: 31 AUG 1998

Received by Reviewer:

Review Completed: 29 JAN 1999

AMENDMENT(S)

Received by CDER: N/A

Received by Reviewer:
Review Completed:

REMARK(S):

The applicant has provided in vitro data to demonstrate the pediculocidal activity of Rid Mousse. The in vitro studies were performed under controlled laboratory conditions, which do not strictly mimic the conditions under in-use conditions. However, the studies were designed to establish the similarity of responses among similar products previously marketed. Within that context, these are meaningful studies; they are not designed to demonstrate efficacy of the product. Efficacy of the product has been assured through the OTC monograph system in which the applicant has demonstrated reasonable similarity to the description within the OTC monograph. These studies provide additional evidence for similarity. The Rid Mousse was tested as formulation 98D11, and its concentrated formulation as 98D12; competitive formulations were also tested as 98D13 and 98D14. Two types of studies were conducted, one for ovicidal activity and another for adulticidal activity against *Pediculus humanis humanis*.

Ovicidal activity was demonstrated by immersion of nit-infested hair with a known number of nits; the raw data were presented on pages 676-680 of the application. After treatment, the nit-infested hairs were subjected to a standardized wash and rinse in tap water. The hairs were blotted dry and then incubated. When the control (sham treated nits) had all hatched, then the remaining nits were counted to see how many hatched. Those unhatched nits represented egg mortality. Unhatched eggs were further characterized microscopically with respect to the stage in which mortality occurred; the microscopic results were tabulated according to the larval stage in which egg development was arrested. Egg development was arrested most frequently in the Late stage of development for the normal Rid Mousse while the Concentrate formulation killed slightly more frequently in the Early stage of development. Most critically, almost no eggs survived to the Emergent state when tested against either Rid formulation or the competitor 98D14 formulation. In contrast, the competitor formulation 98D13 demonstrated marginal activity for killing of the eggs. These marginal results are useful because they serve to corroborate that the test methodology will indeed differentiate among the activities of various formulations.

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Adulticidal activity was demonstrated by a slightly similar series of experiments in which the adults were immersed in the same four test formulations contained within special vials fitted with a screened plunger. The plunger prevented the adults from floating to the surface and thus avoid thorough contact with the test formulation. After treatment, the adults were subjected to a standardized wash and rinse procedure. Subsequently, the adults were evaluated with respect to their remaining capacity to move toward a mild source of heat. Dead adults could not move at all, while moribund adults were only able to move in an ineffectual manner. The final results were tabulated and dead and moribund adults were categorized together as knockdowns; the raw data were presented on pages 699-701 of the application. All four formulations demonstrated 100% knockdown at one hour after treatment. However, continued observation to 24 hours revealed that the knockdown rate for both Rid formulations and competitor 98D13 remained at 100%, but the 98D14 formulation only exhibited 92.7 % knockdown at 24 hours post treatment. The rationale for characterizing moribund adults with dead adults at 24 hours post treatment is that the moribund adults are not capable of feeding and thus die with time. Again, these less efficacious results with the competitor's formulation serve to demonstrate the ability of the test to differentiate among formulations.

The equivalence of Rid Mousse to other competitive monograph products has been demonstrated based on the comparative pediculocidal activity against eggs and adults under the described test conditions. The test conditions were uniformly applied to all test formulations, and the test conditions were adequate to differentiate among the formulations. Clearly, the Rid Mousse formulation has in vitro activity. However, this activity was not clearly correlated with the clinical efficacy of Rid Mousse or any of the other OTC monograph formulations. Approval of a product governed by an existing OTC monograph does not require independent corroboration of clinical efficacy; rather, it is only necessary to demonstrate adequate similarity to other products within that monograph definition. Overall, these studies have demonstrated equivalence to other products marketed under the OTC monograph, but the studies do not establish the clinical efficacy of Rid Mousse.

CONCLUSIONS and/or RECOMMENDATIONS:

The results of comparative in vitro studies have demonstrated the similarity of Rid Mousse to other OTC monograph products approved as pediculocides. The results were obtained using uniform test conditions which could show presumptive differences among the

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test formulations. However, the results do not give a clear understanding of the clinical efficacy of Rid Mousse. Nevertheless, adequate similarity of Rid Mousse has been demonstrated from the in vitro perspective. Overall, Rid Mousse should be considered approvable unless full clinical efficacy data are needed for approval

/S/

6/23/99

✓ James R. King
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SMicro/ASheldon

BD #1 and Final Initialed 6/23/99 ASH

6/23/99

7/7/99

DepDir/LGavrilovich

- cc: dOrig. NDA # 21043
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- HFD-520/SMicro/ASheldon
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- HFD-540/MO/Hu
- HFD-540/Pharm/Reid
- HFD-540/Chem/Yaciw
- OTC/CSO/Merritt
- HFD-520/SCSO/Bona

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**APPEARS THIS WAY
ON ORIGINAL**