

DECLARATION OF KHANH P. TRAN, M.D.

In Support of the Citizen Petition of Valeant Pharmaceuticals International

Docket No. 2004P-0557

Khanh P. Tran, M.D., under penalty of perjury, declares as follows:

1. Valeant Pharmaceuticals International has requested that I comment on the differences between actinic keratosis ("AK") and superficial basal cell carcinoma ("sBCC"), from the perspective of a practicing Dermatopathologist who examines a large number of skin biopsies and excisions.

2. In general, AKs are localized lesions composed of dysplastic (atypical) squamous epidermal cells (keratinocytes). sBCCs are malignant, neoplastic proliferations of keratinocytes from the basal epidermis, which almost always exhibit multifocal growth within the papillary dermis. Anatomically, they are different diseases that exhibit different growth patterns and behavior.

I. Qualifications

3. I am currently a Pathologist with the San Diego Pathologists Medical Group, Inc., and a Staff Pathologist for Scripps Mercy Hospital, Scripps Memorial Hospital, Chula Vista, and SDP outpatient laboratory. My areas of expertise include general surgical pathology, dermatopathology, cytology, autopsy, and laboratory medicine.

4. I received my Bachelor's and Medical Degrees from the University of Oklahoma. I underwent postgraduate training in anatomic and clinical pathology at the Johns

Hopkins Medical Institutions in Baltimore, Maryland, and was awarded fellowships in dermatopathology and surgical pathology at Stanford University Medical Center in Stanford, California.

5. I have been certified in Dermatopathology by the American Boards of Pathology and Dermatology and in Anatomic/Clinical Pathology by the American Boards of Pathology. My *curriculum vitae* is attached at Tab 1.

6. In my practice, during the course of a typical week, I examine between 100 and 150 skin biopsies and excisions. Of these, approximately one-third to one-half exhibit AK or BCC.

II. AK and sBCC Are Disparate Disease Entities

7. AK and BCC are two different disease states. In the former, cumulative exposure to sunlight damages the squamous cells of the epidermis (known as keratinocytes) in a process called dysplasia. These molecular changes lead gradually to a buildup of excess keratin in the epidermis, resulting in pre-malignant lesions. See Tab 2, Figure 1 (histopathologic image of an AK lesion).

8. It is conjectural whether all AKs would eventually evolve into skin cancer (usually squamous cell carcinoma). Indeed, it is likely that many AKs would regress or remain unchanged for many years; however, if left untreated, sufficient numbers of AK lesions would become malignant to warrant local eradication.

9. In contrast, BCC is a malignant neoplasm of the skin. BCCs are the most common skin tumors, accounting for about 70% of all malignant diseases of the skin. Like AK, BCC has a tendency to occur at sites subject to chronic sun exposure and is more common in fair-skinned individuals. BCCs arise from the lowermost layers of the epidermis; a small percentage may originate from the outer root sheath of the hair follicle. Various morphological subtypes of BCC have been defined. One subtype of BCC commonly grows in a pattern known as "multifocal superficial basal cell carcinoma" or "superficial BCC." This subtype accounts for 10-20% of all BCCs.

10. Microscopically, as its full name implies, an sBCC is characterized by multiple islands or aggregates of basaloid keratinocytes, with palisading of the cells at the periphery, which emanate from the undersurface of the epidermis and extend into the papillary dermis. The islands of tumor cells are surrounded by a stroma, which is newly formed and different from the adjacent dermis. The stroma shows some alterations at the molecular level that may facilitate the neoplasm's ability to invade. This multifocal growth pattern is usually not seen with AKs, which do not invade the papillary dermis. See Tab 2, Figure 2 (histopathologic image of an sBCC).

11. Finally, sBCCs typically remain within the papillary dermis, but may extend over several square centimeters or more of skin surface. This multifocal growth pattern may on occasion render evaluation of the tumors' excision margins difficult -- both clinically and on histologic examination. If sBCC is present at the surgical margins, the general practice is to re-excise to ensure complete removal, since sBCC may recur -- and if recurrence does occur, can

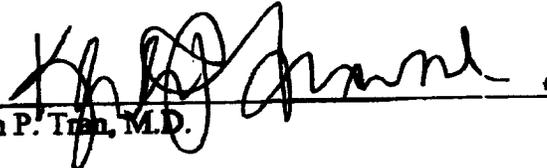
be difficult to control. By contrast, if an AK lesion is not completely removed, most clinicians will not re-excise, because AKs present much less serious complications for patients.

III. Conclusion

12. For these reasons, and based on my medical expertise, I conclude that AK and sBCC are two different diseases, both clinically and under the microscope. AKs are pre-malignant lesions, while sBCC is a malignant skin cancer. sBCC is the more serious condition, for which inadequate treatment can have serious consequences.

I declare under penalty of perjury that the foregoing is true and correct.

Executed in San Diego, California, this 31st day of March, 2006.



Khanh P. Tran, M.D.