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October 26, 2007

BY HAND DELIVERY

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Citizen Petition for Rare Cancer Guidance Document

Dear Sir/Madam:

On behalf of The Alliance Against Alveolar Soft Part Sarcoma ("TAAASPS") and the Sarcoma Foundation of America ("SFA"), enclosed please find a Citizen Petition requesting that the Food and Drug Administration ("FDA") issue a guidance document for the accelerated approval of drugs and biologics that are intended to treat rare cancers, including alveolar soft part sarcoma ("ASPS").

Significant challenges are raised by the research, development, and approval of treatments for rare cancers. As explained in the enclosed petition, these challenges include the rarity of the cancer, small target populations, slow study accrual, evolving standards of care, identification of clinical and/or surrogate endpoints, and level of evidence necessary to obtain approval of a rare cancer treatment, among others. Further clarification and guidelines from FDA on these issues would provide invaluable guidance and facilitate the development and approval of treatments for rare cancers, including ASPS.

TAAASPS and the SFA appreciate the agency's review and action on the enclosed petition and look forward to working with FDA to help make treatments for rare cancers available to patients who desperately need them.

Sincerely,


Peter O. Safir
Heather D. Banuelos
*Counsel for the Sarcoma
Foundation of America*

Enclosure

cc: Andrew C. von Eschenbach, MD
Commissioner of Food and Drug Administration

October 26, 2007

BY HAND DELIVERY

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

**Re: Citizen Petition to Request a Guidance Document to Improve
the Accelerated Approval Process for Drugs and Biologics
Intended to Treat Patients with Rare Cancers**

To whom it may concern:

On behalf of The Alliance Against Alveolar Soft Part Sarcoma (“TAAASPS”) and the Sarcoma Foundation of America (“SFA”), the undersigned submit this petition under 21 C.F.R. § 10.30 to request the Commissioner of Food and Drugs to issue a guidance document to provide specific guidelines under the Food and Drug Administration’s (“FDA” or “the agency”) accelerated approval process for drugs that are intended to treat rare cancers, including alveolar soft part sarcoma (ASPS). Specifically, we request guidelines for approval of any drug or biological product intended to treat a rare cancer that might not yet have an established surrogate endpoint, or that has an established surrogate endpoint but is unable to achieve final approval based upon adequate and well-controlled clinical studies, due to the rarity of the cancer and/or ethical constraints in conducting such studies.

Sarcomas are a rare and diverse group of malignant tumors that develop from fat, muscle, nerves, joints, blood vessels, bones, or other connective or supportive tissues.¹ They constitute about one percent of all adult malignancies, and are more prevalent in children, constituting about 15-20 percent of all childhood malignancies.² ASPS represents 0.05-1.0% of all soft tissue sarcomas. Each year between 50-100 American men, women and children are diagnosed with ASPS. Surgery can be curative in some cases, but there is no approved or known effective

¹ National Cancer Institute, U.S. National Institutes of Health, Dictionary of Cancer Terms, “sarcoma,” available at http://www.cancer.gov/Templates/db_alpha.aspx?CdrID=45562 (last accessed October 24, 2007), attached as Exhibit A. See also National Cancer Institute, A Snapshot of Sarcoma (September 2006), available at <http://planning.cancer.gov/disease/Sarcoma-Snapshot.pdf> (last accessed October 24, 2007), attached as Exhibit B.

² See National Cancer Institute, A Snapshot of Sarcoma, *supra* note 1 (Exhibit B).

therapy for those in whom surgery is not curative. Moreover, studies do not demonstrate benefit from chemotherapy or radiation in the treatment of ASPS.³

TAAASPS is a non-profit organization that was founded in June 2000 to encourage and promote research and funding for ASPS treatments. The mission of TAAASPS is to act as an advocate for increased research to discover therapies to treat patients with ASPS. The SFA is a non-profit organization that was founded in August 2000 to encourage and promote research and funding for, and education and awareness of, sarcoma risks and treatments. The mission of the SFA is to act as an advocate for increased research to discover new and better therapies to treat patients with sarcoma. The SFA raises funds to provide grants to support research focused on discovering and developing new therapies to treat and cure sarcomas. The SFA also interacts with public (e.g., National Cancer Institute), private for-profit (e.g., pharmaceutical companies), and private non-profit (e.g., philanthropic foundations) entities to educate and raise awareness about sarcoma risks and treatment needs of sarcoma patients.

A. Action Requested

TAAASPS and the SFA request that FDA issue guidance pertaining to the accelerated approval process for a drug or biologic intended to treat rare types of cancer, such as ASPS. Specifically, the petitioner seeks the creation and publication of a guidance document that provides criteria for evaluating and satisfying the requirements for a New Drug Application (“NDA”) or Biologics License Application (“BLA”) that seeks or has received accelerated approval under 21 C.F.R. Part 314, Subpart H (for NDAs) or 21 C.F.R. Part 601, Subpart E (for BLAs). The guidance should explain how a NDA for a drug or BLA for a biologic intended to treat a rare cancer could meet accelerated approval requirements, including post-approval Phase IV confirmatory studies, when such cancer (a) might not yet have an established surrogate endpoint, or (b) has an established surrogate endpoint but is unable to achieve final approval based upon adequate and well-controlled clinical studies, due to the rarity of the cancer and/or ethical constraints in conducting such studies.

The requested guidance should address and respond to the challenges inherent in the study and approval of treatments for rare cancers, as identified by the agency’s Oncologic Drugs

³ See, e.g., Portera, C.A., *et al.*, Alveolar Soft Part Sarcoma – Clinical Course and Patterns of Metastases in 70 Patients Treated at a Single Institution, *Cancer*, 2001; 91(3):585-591, attached as Exhibit C. See also Kayton, M.L., *et al.*, Clinical presentation, treatment, and outcome of alveolar soft part sarcoma in children, adolescents, and young adults, *J. Ped. Surgery*, 2006; 41: 187-193, attached as Exhibit D.

Advisory Committee (“ODAC” or “the committee”) in its November 2005 meeting.⁴ This requires consideration of whether treatments for rare cancers should be subject to a separate and distinct risk-benefit evaluation based upon a “constellation of data” different from other drugs or biologics – because randomized controlled clinical trials of rare cancers may not be feasible, rare cancers have very small populations resulting in slow study accrual, clinical endpoints are not always known nor are surrogate endpoints always established, supportive care treatment paradigms are constantly evolving, and long-term studies and/or the use of a placebo or less effective comparator present ethical dilemmas.

B. Statement of Grounds

Section 505 of the Federal Food, Drug and Cosmetic Act (“FDCA” or “the Act”)⁵ and section 351 of the Public Health Service Act (“PHS Act”)⁶ govern the approval processes for NDAs and BLAs, respectively. New drugs will be approved if they meet safety and effectiveness criteria set forth in FDCA section 505(d)⁷ and FDA’s implementing regulations in 21 C.F.R. Part 314. Licenses for biological products may only be issued if they meet standards for the “continued safety, purity, and potency of such products,” as defined by regulation in 21 C.F.R. Part 601.⁸

In 1992, FDA issued regulations specifically governing an accelerated approval process for drugs and biologics.⁹ The agency’s regulations allow for the earlier approval of products that have been “studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit to patients over existing treatments.”¹⁰ Accelerated approval is based upon surrogate endpoints for the targeted cancer, and therefore

⁴ See Notice of Meeting; 70 Fed. Reg. 60094 (October 14, 2005); 70 Fed. Reg. 62126; Amendment of Notice (October 28, 2005). See also Transcript of the Oncologic Drugs Advisory Committee, November 8, 2005 [hereinafter “ODAC Transcript”], available at <http://www.fda.gov/ohrms/dockets/ac/05/transcripts/2005-4191T1.pdf> (last accessed October 24, 2007).

⁵ 21 U.S.C. § 355.

⁶ 42 U.S.C. § 262.

⁷ 21 U.S.C. § 355(d).

⁸ 42 U.S.C. § 262(d).

⁹ See generally 21 C.F.R. Part 314, Subpart H and Part 601, Subpart E.

¹⁰ *Id.* at §§ 314.500, 601.40.

requires that the applicant continue to study the drug post-approval to verify the clinical benefit. The agency's regulations specifically state the following, in relevant part:

FDA may grant marketing approval for a new drug product [or for a biological product] on the basis of adequate and well-controlled clinical trials establishing that the drug product [or the biological product] has an effect on a surrogate endpoint that is reasonably likely, based on epidemiologic, therapeutic, pathophysiologic, or other evidence, to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. Approval ... will be subject to the requirement that the applicant study the drug [or the biologic] further, to verify and describe its clinical benefit, where there is uncertainty as to the relation of the surrogate endpoint to clinical benefit, or of the observed clinical benefit to ultimate outcome....¹¹

Among other things, FDA's accelerated approval regulations provide for restrictions to ensure safe use of the product, as well as withdrawal procedures if, for example, a postmarketing study fails to verify the clinical benefit, or the applicant fails to conduct the required postmarketing studies.¹² In 1997, Congress passed the Food and Drug Administration Modernization Act of 1997 ("FDAMA"),¹³ which, in effect, codified FDA's accelerated approval provisions.

Since the implementation of FDA's accelerated approval regulations, it has become clear that the process is problematic for drugs and biologics intended to treat rare cancers. Clinical development programs for rare cancers have become increasingly difficult to conduct and complete, almost as a direct function of the rarity of the cancer and only in part modulated by aspects of each trial design and history. The challenges inherent in these clinical development programs and FDA's accelerated approval process were highlighted during the FDA ODAC meeting of November 8, 2005, in which FDA charged the committee "to consider the following for ongoing [Phase IV] confirmatory studies: has accrual been satisfactory? If not, what strategies do you suggest for improvement? ... Please discuss the relative merits of different trial designs and patient populations for accelerated approval ... [and] provide any other suggestions for improving the accelerated approval process as a whole."¹⁴

¹¹ *Id.* at §§ 314.510, 601.41.

¹² *Id.* at §§ 314.520, 314.530; 601.42, 601.43.

¹³ *See* 21 U.S.C. §§ 355(c), 356(b).

¹⁴ *See* ODAC Transcript, *supra* note 4, at 31-32.

At the end of that meeting, ODAC members considered whether they should create a consensus document of the committee's views on the issues and problems raised by the accelerated approval of treatments for rare cancers. Although FDA welcomed the committee members' views, the agency did not necessarily support a formal ODAC consensus paper, primarily because the agency believed it might be difficult to capture the various views of all committee members. FDA also explained that the transcript and recording of the meeting serve to communicate the committee's advice.¹⁵

Because the November 2005 ODAC did not issue any consensus document, nor did it vote on any specific questions related to accelerated approvals in the rare cancer context, TAAASPS and the SFA consider it critical to cite the manner of the ODAC's advice for implementation by FDA. The issues raised by the committee that day continue to be of vital importance to rare cancer patients such as children and adults with sarcoma, as well as to research entities seeking to develop new treatments for rare cancers, including ASPS. Therefore, we refer to and rely upon the various statements at that meeting, as evidenced by the ODAC Transcript of November 8, 2005,¹⁶ as the guiding advice to FDA on this topic, and as the basis of our request for clear guidance about how to overcome significant obstacles in the accelerated approval process for drugs or biologics intended to treat rare cancers.

The accelerated approval process presents a number of challenges to NDAs and BLAs for rare cancer treatments due to the unique nature of the cancer and affected populations.¹⁷ The ODAC recognized that these challenges include the rarity of the cancer and small population size, slow study accrual, length of studies, evolving standards of care and treatment paradigms, identifying clinical or surrogate endpoints, study design, and the level of evidence necessary to obtain approval.

As previously mentioned, ASPS is a rare cancer, having approximately 50-100 new diagnoses each year and no effective treatment.¹⁸ In comparison to other cancers, rare cancers like ASPS affect only a small percentage of the overall population. This small population size is the first challenge to the research and development of a rare cancer treatment.¹⁹ The number of

¹⁵ *Id.* at 356-63.

¹⁶ *See* ODAC Transcript, *supra* note 4.

¹⁷ Despite these challenges, we acknowledge Ariad's recent initiation of a global Phase III clinical trial of oral deforolimus in patients with metastatic soft tissue and bone sarcomas.

¹⁸ *See* Portera, C.A., *et al.*, Alveolar Soft Part Sarcoma, *supra* note 3 (Exhibit C); Kayton, M.L., *et al.*, Clinical presentation, treatment, and outcome of alveolar soft part sarcoma in children, adolescents, and young adults, *supra* note 3 (Exhibit D).

¹⁹ *See* ODAC Transcript, *supra* note 4, at 128, 155-56, 327.

patients affected by ASPS or other rare cancers necessarily limits the rate of accrual in a clinical study. Few clinical research centers in any country see a significant number of patients with rare cancers,²⁰ despite the fact that there are nearly 1,000 cancer diagnoses that can be considered rare.²¹ Moreover, even if they did, the patient would nevertheless need to meet inclusion criteria to be considered an appropriate study participant.²²

Study designs also present challenges in the accelerated approval of rare cancer treatments. For example, study designs may affect accrual rates because patients may be less willing to participate in a randomized, placebo-controlled study for fear of being given a placebo in lieu of the approved drug.²³ Thus, the continued approval of a product can become a critical problem in being able to complete and obtain further information.²⁴ Further, randomized or controlled studies are not always feasible or may not produce reliable results due to delays in accrual, study conduct, and/or evolving treatment paradigms or standards of care. One ODAC committee member stated that “for some of the randomized trial designs with placebo control the accrual is so slow that we never [achieve substantial evidence].”²⁵ Indeed, Dr. Pazdur of the FDA questioned whether the degree of evidence required for approval of rare cancer treatments should be different:

DR. PAZDUR: “Now, for rare cancers we have looked at what is substantial evidence to warrant approval and, obviously that may be based [] on [a] different risk and benefit decision. . . . [Q]uestions I think people need to answer is do they have adequate information for approval? Will they ever have that? Could we, for example, because this is a relatively unusual population, take a look at a different risk/benefit relationship here?”²⁶

In light of these concerns, some ODAC members suggested that the committee and the agency consider different study designs to support the approval of rare cancer treatments, including the use of an observational or prospective cohort study:

²⁰ *Id.* at 129.

²¹ Raretumors.org, Rare Tumors List, available at <http://www.raretumors.org/list.asp> (last accessed October 24, 2007), attached as Exhibit E.

²² ODAC Transcript, *supra* note 4, at 129.

²³ *Id.* at 327.

²⁴ *Id.* at 145-46.

²⁵ *Id.* at 327.

²⁶ *Id.* at 231 (emphasis added).

DR. RODRIGUEZ: "We have been talking about the type of data that would be required in very small patient populations I wonder if perhaps in cancers that are very rare a different data source might be considered or a different strategy for data collection be considered along the lines of a registry, along the lines of a tumor registry which can be coordinated with the drug companies So perhaps in [a] very limited number of patients where a randomized trial does not work for data acquisition, prospective cohort data might be the best we can do."

....

DR. CHESON: "... It is possible that that sort of mechanism could be used even post-approval if you had agreement ... from the physician to do it, send that protocol and just have some follow-up and you could probably get those data."

DR. MARTINO: "But inherent in these concepts is the assumption that that data would meet some rigor that the FDA would find acceptable...."²⁷

ODAC member Dr. George also supported the concept of registry-based studies for rare cancer treatments, but clarified that such a study should be "more like a clinical trial, with the treatments being carefully defined, the results all being carefully analyzed in a protocol, and particular eligibility criteria," such that "the only difference between that and a real ... randomized clinical trial would be the assignment of the treatment"²⁸

FDA regulations provide that postmarketing studies for accelerated approval must not only be adequate and well-controlled, but must also be carried out with due diligence.²⁹ ODAC members recognized, however, that "due diligence" may be impractical, if not impossible, in studies of rare cancer treatments. One ODAC member, the patient representative, explained that it was important to "anticipate [the study enrollment] issue in realistically predicting whether or not trials can be carried through to completion."³⁰ Another ODAC member stated:

DR. MARTINO: "Given everything you have heard and everything you know, do we actually think that a randomized trial in this cancer that would answer issues of time to progression,

²⁷ *Id.* at 233-35.

²⁸ *Id.* at 283-84.

²⁹ 21 C.F.R. §§ 314.510, 601.41.

³⁰ ODAC Transcript, *supra* note 4, at 155.

survival – do we think that that can be done?...[C]an we expect additional information in a timely manner that will satisfy the needs?”³¹

It was equally noted that “the longer it takes to complete the commitment, the less relevant the results are.”³² The length and reliability of the study are also affected by poor or outdated comparators. For example, with a slow rate of accrual, there may be changing and evolving supportive care treatment paradigms.³³

ODAC members also acknowledged the ethical issues raised by slow accrual, long-term studies, and/or the use of a placebo or less effective comparator in rare cancer clinical studies.³⁴ For example, the “impact of a placebo arm in a symptomatic population is very important,” particularly where the drug is already approved or there are other available treatment options.³⁵

The recognition of established clinical or surrogate endpoints for the study of rare cancers also presents a challenge in the accelerated approval process. FDA defines a “surrogate endpoint” as:

a laboratory measurement or physical sign that is used in therapeutic trials as a substitute for a clinically meaningful endpoint that is a direct measure of how a patient feels, functions, or survives and that is expected to predict the effect of the therapy.³⁶

Of course, the “use of a surrogate endpoint can considerably shorten the time required prior to receiving FDA approval” of a drug or biologic.³⁷ However, in many instances of rare cancers, an established surrogate endpoint is not even known. In other instances, surrogate endpoints are established, but it is not possible to continue with adequate and well-controlled Phase IV confirmatory studies. Because clinical and/or surrogate endpoints are not always clear or

³¹ *Id.* at 94-95.

³² *Id.* at 318.

³³ *Id.* at 155, 318-319.

³⁴ *E.g., id.* at 317-19.

³⁵ *Id.* at 129.

³⁶ 57 Fed. Reg. 13234 (April 15, 1992).

³⁷ FDA, Fast Track, Accelerated Approval and Priority Review (May 2006), *available at* <http://www.fda.gov/oashi/fast.html> (last accessed October 24, 2007).

established for rare cancers, it becomes more difficult to evaluate the effectiveness of a treatment under the requirements of the FDCA, PHS Act, and FDA's implementing regulations. In May 2007, FDA issued final guidance concerning clinical trial endpoints for the approval of cancer drugs and biologics.³⁸ Unfortunately, this guidance does not address the endpoint challenges that are unique to the study of rare cancers. An agency representative posed the following questions on this issue during the November 2005 ODAC meeting:

DR. DAGHER: [T]he kind of endpoint that you consider most relevant really does depend on the cancer setting. So, just because we may not use tumor shrinkage in and of itself as evidence of clinical benefit in, say, some of the solid tumors, that doesn't mean it applies across the board [W]e want suggestions on really where do we go from here. Is there some totality of evidence? Is there an additional study that could be done to really focus on the questions that have not been answered? Again, that does not necessarily have to be a huge randomized trial. So, I guess what I am trying to get at is ... where do we go from here really. Is it a new study? If so, what is the design of that study? If not, what is the totality of evidence that we have? Again, we have said that the problem of going with that route is that even with some of the data that is out there, it is questionable how much you can document that when it is time for FDA to review that data.³⁹

These challenges and concerns in the context of accelerated approvals of rare cancer treatments ultimately raise a question about the scope of evidence required for approval. In light of these challenges, some members of the ODAC questioned whether alternative datasets to randomized, controlled trials could be used to obtain approval,⁴⁰ and whether a separate and distinct risk-benefit evaluation based upon the "totality of evidence" or a "constellation of data" different from other drugs or biologics might serve as the basis for approval of rare cancer treatments.⁴¹ In essence, the committee considered, and in some cases encouraged, that "the

³⁸ FDA Guidance for Industry: Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics (May 2007), *available at* <http://www.fda.gov/cber/gdlns/clintrialend.pdf> (last accessed October 24, 2007).

³⁹ ODAC Transcript, *supra* note 4, at 96-97 (emphasis added).

⁴⁰ *Id.* at 233-35.

⁴¹ *Id.* at 97-98, 327.

requirements to giving accelerated approval [to rare cancer treatments] should be somewhat different”⁴² For example,

one could envision setting up a body of data requirements for full approval of these agents, and that could be a constellation of data that doesn’t necessarily have to be randomized but needs to be done in a high quality manner that could be partnered with FDA.⁴³

In conjunction with these considerations, committee members referenced European initiatives, including the European Community marketing authorization under exceptional circumstances and the advent of the European Community conditional marketing authorization, the latter granted by the European Commission following review by the European Medicines Agency (“EMA”).⁴⁴ In short, the EMA’s Conditional Marketing Authorisation (“CMA”) is similar to FDA’s accelerated approval process in that it is granted before all data are available; however, the CMA is only valid for one year, subject to renewal.⁴⁵ Like FDA’s accelerated approval process, the CMA is intended to ultimately be completed with all necessary scientific data to establish safety and efficacy. On the other hand, the European Commission (following review of an application by the EMA) and the national medicines regulators in each European Union member state may grant a marketing authorization under exceptional circumstances when an applicant demonstrates that he is unable to provide comprehensive data on the safety and efficacy of a product under normal conditions of use – because (a) the indications for the product are so rare that comprehensive evidence cannot be reasonably expected; (b) comprehensive information cannot be provided in the present state of scientific knowledge; or (c) it would be unethical to collect such information.⁴⁶ Such authorization is granted subject to the requirement

⁴² *Id.* at 231-32.

⁴³ *Id.* at 327 (emphasis added).

⁴⁴ *See, e.g., id.* at 230-32.

⁴⁵ Commission Regulation 507/2006, 2006 O.J. (L 92/6), attached as Exhibit F. *See also* EMA Human Medicines – EMA Pre-Submission Guidance, Questions & Answers, 44. Could my application qualify for a conditional marketing authorization?, *available at* <http://www.emea.europa.eu/htms/human/presub/q44.htm> (last accessed October 24, 2007), attached as Exhibit G.

⁴⁶ Commission Regulation 726/2004, art. 14(8), 2004 O.J. (L 136/1), attached as Exhibit H; Council Directive 2001/83/EC, as amended, art. 22, 2001 O.J. (L 311/67), attached as Exhibit I; Directive 2003/63/EC, Annex I, Part II, § 6, 2003 O.J. (L 159/46), attached as Exhibit J; EMA, Committee for Medicinal Products for Human Use, Guideline on Procedures for the Granting of a Marketing Authorisation Under Exceptional Circumstances, Pursuant to Article 14(8) of Regulation (EC) No. 726/2004 (December 15, 2005), attached as Exhibit K. *See also* EMA Human Medicines – EMA Pre-Submission Guidance, Questions & Answers, 32. Marketing (continued...)

that the applicant comply with specific obligations or conditions, which may include completion of identified studies, restrictions on the distribution and administration of the product, and labeling that notifies a healthcare practitioner of the “exceptional” status of the product.⁴⁷ Unlike the CMA, which is renewed formally each year, the marketing authorization under “exceptional circumstances” is subject to an annual review to reassess the risk-benefit balance.

Members of the ODAC considered the “conditional” aspects of the EMEA’s marketing authorization, favoring “conditional” approval over FDA’s “accelerated” approval.⁴⁸ In addition, some ODAC members encouraged further consideration of the “exceptional circumstances” approval and suggested that different data could be considered for approval of treatments for rare cancers. For example:

DR. PERRY: “... I think that we do need to set a bar that says if you have a Phase 2 study with X level of expectation done by a responsible group, with the data audited, I think you might be able to proceed from there without having to go through a Phase 3 trial.”⁴⁹

It was also recommended that FDA consider withdrawing or not enforcing the requirement of Phase IV confirmatory studies for treatments for rare cancers and small target populations.⁵⁰

Since the November 2005 ODAC meeting, FDA has not taken a consistent review approach towards applications focusing on rare cancers. For example, in October 2006, Novartis obtained full approval for five additional rare cancer indications for Gleevec® (imatinib mesylate) based on molecular biological mechanistic data and clinical trial data on only a few dozen patients. The approval of Gleevec for these rare cancer indications appears very much in keeping with the advice and recommendations of the ODAC. However, in mid-2007, FDA denied IDM Pharma’s NDA for mifamurtide (L-MTP-PE) based on immune system mechanistic data, supported by overall survival data in several hundred osteosarcoma patients.

authorization under exceptional circumstances, *available at* <http://www.emea.europa.eu/htms/human/presub/q32.htm> (last accessed October 24, 2007), attached as Exhibit L.

⁴⁷ See EMEA, Committee for Medicinal Products for Human Use, Guideline on Procedures for the Granting of a Marketing Authorisation Under Exceptional Circumstances, Pursuant to Article 14(8) of Regulation (EC) No. 726/2004, *supra* note 46 (Exhibit K).

⁴⁸ See, e.g., ODAC Transcript, *supra* note 4, at 79-80, 328-29, 333.

⁴⁹ See *id.* at 328, 334.

⁵⁰ *Id.* at 339.

As the November 2005 ODAC meeting progressed, and as TAAASPS and the SFA have considered the pertinent issues, in light of the FDA's accelerated approval process and challenges inherent in the research and development of treatments for rare cancers, the question is ultimately about what evidence will support approval for treatments for rare cancers⁵¹ and how FDA can accommodate such treatments under its current authority, regulations, or enforcement policies. We believe that the overall message from the ODAC meeting nearly two years ago was a resounding call for a change in the status quo. TAAASPS and the SFA support the ODAC's recommendations and advice and request that FDA develop clear guidance to effectively address these important issues.

C. Environmental Impact

The petitioners claim a categorical exclusion from the requirement for submission of an environmental assessment pursuant to 21 C.F.R. § 25.30(h).

D. Economic Impact

The petitioners believe that an economic impact statement may not be necessary for this petition; however, the petitioners agree to provide a statement on the effect of the requested action if one is requested by the Commissioner.

E. Certification

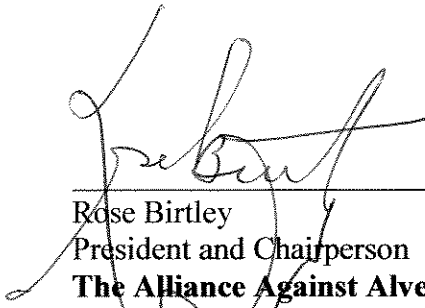
I certify that, to my best knowledge and belief: (a) this petition includes all information and views upon which the petition relies; (b) this petition includes representative data and/or information known to the petitioner which are unfavorable to the petition; and (c) I have taken reasonable steps to ensure that any representative data and/or information which are unfavorable to the petition were disclosed to me. I further certify that the information upon which I have based the action requested herein first became known to the party on whose behalf this petition is submitted on or about the following date: November 8, 2005 (ODAC Meeting). I have not

⁵¹ *Id.* at 329.

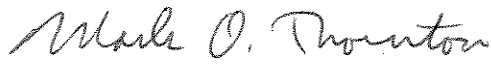
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received nor expect to receive payments, including cash and other forms of consideration, to file this information or its contents, from any person or organization. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.

Respectfully submitted,



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Attachments

cc: Andrew C. von Eschenbach, MD
Commissioner of Food and Drug Administration