UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

DIVISION OF
CORPORATION FINANCE

May 6, 2011

Joseph Pandolifino
Chief Executive Officer
22nd Century Group, Inc.
8201 Main Street, Suite 6
Williamsville, NY 14221

Re: 22nd Century Group, Inc.
Registration Statement on Form S-1
Filed April 11, 2011
File No. 333-173420

Dear Mr. Pandolifino:

We have limited our review of your registration statement to those issues we have addressed in our comments. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter by amending your registration statement and providing the requested information. Where you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing any amendment to your registration statement and the information you provide in response to these comments, we may have additional comments.

General

1. Given that there is no guarantee that X-22 or Brand A and Brand B will obtain the necessary approval from the FDA, please revise significantly throughout to clarify this and to provide more balanced disclosure regarding your potential products. Please also revise to clarify that there is no guarantee that you will qualify for "Fast Track" designation. In addition, please clarify throughout that the FDA has yet to release its regulations regarding modified risk cigarettes and that, as of June 2010, all cigarette companies were required to cease the use of the terms "low tar," "light" and "ultra light."

2. Please revise to clarify what you mean by the phrases "super-premium priced cigarette brands," "specialty cigarette components," "full flavor cigarette brands," "reduce smoke exposure," "biomass products" and "bioconversion."

Registation Statement Cover Page

3. The registration fee appears to have been calculated pursuant to Rule 457(c) of the Securities Act. Please revise footnote 2 to the Calculation of Registration Fee table or advise.

Our Company, page 1
Overview, page 1

4. Please include in one of your introductory paragraphs your revenues, assets, and losses for the most recent audited period and interim stub. This snapshot will help investors evaluate the disclosure as they read the filing. Also, disclose the fact that your independent auditor's report expresses substantial doubt about your ability to continue as a going concern and that you will not receive any proceeds from this offering.

5. Please revise the first paragraph on page one to clarify that you have not attempted to obtain approval or authorization for your products outside of the United States and that there is no guarantee that you will be able to gain approval or authorization for your products outside of the United States.

6. We note your statement on page one that you plan to use a substantial portion of the proceeds of the Private Placement Offering to complete clinical trials for X-22. Please revise to provide quantitative information here regarding the cost of completing these trials, the amount of money raised in the Private Placement Offering. In addition, please either define the term "Private Placement Offering" or include a cross-reference to the definition.

7. Please revise your discussion of the clinical trials for X-22 and your plans to produce and sell modified risk cigarettes by adding the disclosure from the last risk factor on page eight that the net proceeds of the Private Placement Offering will not be sufficient to enable you to complete the FDA approval process for X-22 or the FDA authorization process for your Modified Risk Cigarettes and that you will have to seek additional funding to complete your business plans.

8. Please provide support for your statement on page one that X-22 is the only smoking cessation product that functions exactly like a regular cigarette and your statement on page three that the modifications you have made to your proprietary tobacco do not affect the leaf constituents important to a cigarette's characteristics, including taste and aroma.

RED SUN and MAGIC Cigarettes, page 2

9. Please provide support to us for your statement that the ban of flavored cigarettes has created a product void in the tobacco channels where you intend to focus your marketing efforts. Alternatively, please revise to state that this is your belief.

Technology Platform and Intellectual Property, page 3

10. Please balance your disclosure regarding your intellectual property on page three with your disclosure in the last risk factor on page 18 and in the second to the last risk factor on page 19 that you have not performed searches for third-party intellectual property rights that may raise freedom-to-operate issues, that you have not obtained legal opinions regarding the commercialization of your potential products and that there may be existing patents that affect your ability to commercialize your potential products.

Recent Developments, page 3

11. Please revise to clarify the manner in which you sold 5,434,446 Private Placement Offering Securities in the Private Placement Offering and how this relates to the shares being offered. Additionally please reconcile the statement on page three regarding "each Unit consisting of one limited liability company membership interest of 22nd Century and a five-year warrant to purchase one half of one (1/2) limited liability company membership interest" with the statement on page 32 regarding "each such PPO Security consisting of one (1) Unit and a five-year warrant to purchase one-half of one (1/2) Unit."

Risk Factors, page 7

12. Refer to the third sentence in the introductory paragraph to this section. All material risks should be discussed in this section. If risks are not deemed material then they should not be mentioned. Please revise accordingly.

13. We note your statement in the last paragraph on page 35 that Vector Tobacco had previously marketed Quest cigarettes. Please provide an appropriate risk factor addressing, if true, that at least one of your products was previously marketed unsuccessfully.

Risks Related to Our Business and Operations, page 7

The net proceeds of the Private Placement Offering will not be sufficient to enable us to, page 8

14. Please revise to include an estimate of the cost of completing the FDA approval process for X-22 and, if possible, for your modified risk cigarettes.

Risks Related to Ownership of Our Common Stock, page 20

We will incur increased costs and demands upon management as a result of complying, page 21

15. We note your disclosure in this risk factor that you are currently unable to estimate the costs of complying with the laws and regulations for public companies. However, you

are currently a reporting company and must already comply with the laws and regulations affecting public companies. Please revise or advise.

An active trading market for our common stock may not develop or be sustained, and, page 21

16. Please reconcile your disclosure here with your disclosure on the cover page of your prospectus that your common stock is currently traded on the OTC Bulletin.

A significant portion of the total outstanding shares of common stock may be sold into, page 22

17. Please provide a definition for "PPO Security" and "EIP" here.

18. Please revise the first sentence in the second paragraph of this risk factor to clarify that the shares can be sold in the public market after the effective date of the registration statement.

We are controlled by our current officers, directors and principal stockholders, page 23

19. Please reconcile your disclosure here that your directors and officers own 33.8% of the outstanding shares of your common stock with your disclosure on page 26 that they own 39.50% of the outstanding shares of your common stock or advise.

Business, page 32

Overview, page 32

20. Please provide a basis for statements such as "a global leader" and "will enable us to capture a significant share of the global market…" on page 32 and "well-positioned to capture a significant share of this market" and "expand the smoking cessation market" on page 33.

21. We note your disclosure that you own or exclusively control 98 issued patents. Please revise to clarify the number of patents that you hold and, to the extent material, please disclose the duration of your patents and licenses.

Market, page 34

22. Please revise the reference to the Datamonitor forecast in the last paragraph on page 34 to indicate the first date covered by the forecast. If it is not a recent forecast please tell us why the forecast is still reliable.

Modified Risk Tobacco Products, page 35

23. Please revise to provide support for your statement in the last sentence in the first paragraph on page 36.

Products, page 36

X-22 Smoking Cessation Aid, page 36

24. Please balance your statement that you plan to complete the FDA-approval process for your X-22 smoking cessation aid in the fourth quarter by adding your disclosure from the first complete risk factor on page 13 that the time required for FDA approval and authorization is lengthy and uncertain.

Brand A Cigarettes, page 37

25. Please refer to the third paragraph. Given that smokers in the study decreased the number of VLN cigarettes they smoked during the six week period, please address the possibility that this means smokers might not be interested in smoking the product in the long term.

Sales and Marketing, page 43

26. Please revise to disclose when you intend to begin marketing each product and the expected cost. Additionally we note references elsewhere to foreign markets. Please clarify for investors whether you have current plans to market internationally, including timelines and costs as applicable.

Government Research Cigarettes, page 44

27. We note your disclosure on page 44 that "you expect to receive an additional purchase order for an additional 7.85 million SPECTRUM research cigarettes in 2011." Please disclose here and elsewhere as appropriate that there is no guarantee that you will receive this order or other direct orders from researchers or advise.

Healthcare Reimbursement, page 44

28. Please revise the second to the last sentence on page 44 to state that it is your belief that you will have latitude in pricing X-22. In addition, please revise the last sentence on page 44 to state that it is your belief that the price of X-22 will not only encourage governmental and private third-party payers to cover X-22 but will also encourage smokers to attempt to quit X-22. Alternatively, please remove these statements.

Clinical Phase, page 47

29. Please revise your discussion to explain how the Phase II-B clinical trials fit into the process described in this section.

X-22 Clinical Trials, page 48

30. Please revise to disclose the amount of additional funding you will need to complete the Phase III clinical trials and whether you have any plans for raising such funding.

Biomass Products, page 49

31. Please revise to clarify what you mean by "once we have achieved success with X-22 and our Modified Risk Cigarettes" on page 49.

32. Please revise the third paragraph on page 50 to state that it is your belief that Rubisco will compete favorably in the markets you list on page 50. In addition, please revise the last sentence in the second to the last paragraph of this section to state that it is your belief that protein concentrates from Verfola will compete favorably in animal feed.

Management's Discussion and Analysis of Financial Condition and Results of Operations, page 52

Net Cash From Financing Activities, page 55

33. We note your disclosure on page 1 that you plan to use a substantial portion of the proceeds from the Private Placement Offering to complete your Phase II-B clinical trial. Please advise as to whether these funds will be sufficient to cover the costs associated with your Phase II-B clinical trial if you are unsuccessful with your negotiations for deferred payment arrangements relating to approximately $1,300,000 owed to NCSU and the two vendors you disclose on page 55. To the extent that these funds will be insufficient to cover your Phase II-B clinical trials if you are unsuccessful in the negotiations with NCSU and the vendors, please disclose on page 1 and add a risk factor that discloses this risk. Please also provide risk factor disclosure regarding any other effects of defaulting on your obligations.

Director Compensation, page 59

34. Please revise this section to include a director compensation table pursuant to Item 402(r) of Regulation S-K.

Executive Compensation, page 59

35. Please revise to include the compensation of Mr. Rector, Mr. Warman, and Mr. Asirwatham. For guidance, refer to Regulation S-K Compliance and Disclosure Interpretations 217.02 and 217.12, available at www.sec.gov. Additionally please revise your Summary Compensation Table on page 59 to include Mr. Rider's compensation.

Director Compensation, page 60

36. Please reconcile your disclosure regarding director compensation on page 60 with your disclosure regarding director compensation on page 59.

Certain Relationships and Related Transactions, page 61

37. We note your disclosure on page 62 regarding shares of your common stock issued to Dr. Moynihan in lieu of cash due and payable to him as compensation. Please disclose this information as footnotes to your Summary Compensation Table on page 59, as applicable.

Exhibits

38. Please file your agreement with RTI international as an exhibit to your next amendment, or please advise.

Other

39. The financial statements should be updated, as necessary, to comply with Rule 3-12 of Regulation S-X.

We urge all persons who are responsible for the accuracy and adequacy of the disclosure in the filing to be certain that the filing includes the information the Securities Act of 1933 and all applicable Securities Act rules require. Since the company and its management are in possession of all facts relating to a company's disclosure, they are responsible for the accuracy and adequacy of the disclosures they have made.

Notwithstanding our comments, in the event you request acceleration of the effective date of the pending registration statement please provide a written statement from the company acknowledging that:

- should the Commission or the staff, acting pursuant to delegated authority, declare the filing effective, it does not foreclose the Commission from taking any action with respect to the filing;

- the action of the Commission or the staff, acting pursuant to delegated authority, in declaring the filing effective, does not relieve the company from its full responsibility for the adequacy and accuracy of the disclosure in the filing; and

- the company may not assert staff comments and the declaration of effectiveness as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

Please refer to Rules 460 and 461 regarding requests for acceleration. We will consider a written request for acceleration of the effective date of the registration statement as confirmation of the fact that those requesting acceleration are aware of their respective responsibilities under the Securities Act of 1933 and the Securities Exchange Act of 1934 as they relate to the proposed public offering of the securities specified in the above registration statement. Please allow adequate time for us to review any amendment prior to the requested effective date of the registration statement.

Please contact Sonia Bednarowski at (202) 551-3666 or me at (202) 551-3859 with any questions.

Sincerely,

John Dana Brown
Attorney-Advisor

cc: Via facsimile: (617) 342-4001
Paul D. Broude
Foley & Lardner LLP