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

DIVISION OF
CORPORATION FINANCE

June 22, 2011

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

Re: 22nd Century Group, Inc.
Amendment No. 1 to Registration Statement on Form S-1
Filed June 7, 2011
File No. 333-173420

Dear Mr. Pandolifino:

We have reviewed your responses to the comments in our letter dated May 6, 2011 and have the following additional comments. All page numbers below correspond to the marked version of your filing.

General

1. We note statements throughout regarding the effectiveness of the products you are developing. Please tell us whether such statements are appropriate given that you have not yet completed the FDA approval process. Additionally please tell us your basis for statements throughout regarding the limited effectiveness or side-effects of competing products.

Registration Statement Cover Page

2. Please revise to indicate the Primary Standard Industrial Classification Code as 2111 or advise.

Prospectus Summary, page 1

Our Company, page 1

Overview, page 1

3. We note your response to our prior comment 33. Please revise to state here that you are currently in default pursuant to the terms of your exclusive worldwide license agreement with North Carolina State University. Please indicate that if NCSU chooses to invoke any right it may have to terminate the License Agreement and you are unable to cure the default, your business would be materially and adversely affected. Please additionally

state that if NCSU does not agree to continue to defer payment of the balance, you may not have sufficient funds to pay for the Phase II-B clinical trial for X-22 in full.

4. We note your response to our prior comment four and reissue in part. Please revise to include your net loss from your most recent interim stub and audited period.

5. We note your response to our prior comment eight and reissue in part. Please provide support to us for your statement on page 2 that X-22 is the only smoking cessation product that functions exactly like a regular cigarette.

6. Please provide support to us that every FDA-approved smoking cessation aid since the establishment of the Fast Track program in 1997 has received the Fast Track designation. Alternatively, please remove this statement.

7. Please revise the last sentence in the second paragraph on page 4 to clarify that you do not have an agreement with RTI or other researchers to purchase additional SPECTRUM cigarettes.

8. Please provide support to us for your statement on page 4 that your tobacco contains the lowest nicotine content of any tobacco ever commercialized. Alternatively, state this as a belief.

9. We note your statement on page 4 that "analyses by an independent accredited laboratory found that the levels of certain compounds in the tobacco leaf of the genetically engineered variety were not substantially different than that of conventional tobacco, except for reduction in nicotine and related compounds." Please state as to whether the report containing these analyses is publicly available. In addition, if this report was not available for free or for a nominal fee, please provide a consent of the author to be named in the registration statement under Rule 436 of the Securities Act of 1933.

10. We note your disclosure in the fourth paragraph on page 4 that you expect your patent applications to cover your products until 2024 to 2026. Please revise to clarify that there is no guarantee that the patent applications will cover your products.

11. We note your response to our prior comment 11. Please revise the statement on page F-16 regarding "each such PPO Security consisting of one (1) Unit and a five-year warrant to purchase one-half of one (1/2) Unit at an exercise price of $1.50 per whole Unit" accordingly.

Risk Factors, page 8

12. We note your response to our prior comment 12 and reissue. Please remove the words "although there may be other risks that could arise or may prove to be more significant than expected, that may affect our operation or financial results" from the third sentence

of the introductory paragraph of this section, and please remove the fourth sentence from the introductory paragraph of this section. If risks are not deemed material then they should not be mentioned.

13. We note your response to our prior comment 13. Please tell us what consideration you have given to providing a risk factor addressing that this product when marketed previously resulted in "relatively low" sales volume.

We will incur increased costs and demands upon management as a result of complying, page 22

14. Please revise to disclose the costs associated with complying with the laws and regulations affecting public companies.

Business, page 33

Overview, page 33

15. We note your response to our prior comment 20. Please further provide us a basis for your belief that you "will enable us to capture a significant share of the global market for approved smoking cessation aids and the emerging market for modified risk tobacco products." Additionally, please revise the second paragraph on page two to indicate that there is no guarantee that you will be able to "take sales and market share from existing smoking cessation products" and "expand the smoking cessation market."

16. We note your response to our prior comment 21 and reissue. Please revise to clarify the number of patents that you own and the number of patents that you license. In addition, please revise to clarify what you mean on page 33 that your "two worldwide exclusive licenses expire upon the last-to-expire patent on a country-by-country basis."

Market, page 36

17. We note your response to our prior comment 22 and reissue in part. Please tell us why the 2008 Datamonitor forecast in the second paragraph on page 36 is still reliable.

Products, page 37

X-22 Smoking Cessation Aid, page 37

18. Please revise the second to the last sentence in the second paragraph on page 38 to clarify that you have not taken any steps to obtain approval for X-22 outside of the United States.

Brand B Cigarettes, page 39

19. Please revise the statement in the second paragraph on page 40 that "[w]e believe that evaluation of BRAND B in short-term human exposure studies will confirm…" given that these studies have not been completed.

Sales and Marketing, page 45

X-22 Smoking Cessation Aid, page 45

20. We note your disclosure on page 45 that you intend to enter into arrangements in both the U.S. and international markets with pharmaceutical companies to market X-22 before completion of the Phase III clinical trials. Please revise to disclose whether you have identified any countries where you intend to attempt to have X-22 approved for commercial sale. Additionally, please include timelines and costs for this international expansion.

21. Please revise to clarify what you mean by "measured approach" in the first paragraph of this section. In addition, please revise the references to "wherewithal" on page 45 to indicate more clearly what resources licensing parties will be required to have.

Brand A and Brand B, page 45

22. We note that you expect to begin marketing your Brand A and Brand B cigarettes internationally in approximately 2 years. Please revise to disclose where you intend to sell your products and advise as to whether you will need to go through an approval process to sell your Brand A and Brand B cigarettes in such countries. To the extent that you will need to obtain approval, please disclose.

Government Research Cigarettes, page 46

23. We note your response to our prior comment 27 and reissue in part. Please revise here and in the second paragraph on page four to clarify that there is no guarantee that you will receive additional orders from RTI or from other researchers or advise.

Potential Smoking Cessation Aids, page 47

24. Please provide support to us for your disclosure in the third paragraph on page 47 regarding the vaccine treatment tests. In addition, please tell us why Dr. Fiore's estimate regarding the approval of a nicotine vaccine in 2009 is reliable.

X-22 Clinical Trials, page 51

25. We note your response to our prior comment 30 and reissue in part. Please revise to disclose whether you have any plans for raising the additional funding you will need for the Phase III clinical trials.

Biomass Products, page 52

26. Please revise to disclose a brief description of your biomass business plan, including a timeline and costs.

Exhibit Index, page E-1

27. Please revise to include all of the exhibits that are included in your registration statement here.

Exhibit 5.1

28. Please have counsel revise the last paragraph of the opinion letter by removing the first sentence as it is inappropriate to limit reliance.

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: (414) 297-4900
Patrick G. Quick
Foley & Lardner LLP