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

DIVISION OF
CORPORATION FINANCE

July 14, 2011

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

Re: 22nd Century Group, Inc.
Amendment No. 2 to Registration Statement on Form S-1
Filed June 29, 2011
File No. 333-173420

Dear Mr. Pandolifino:

We have reviewed your responses to the comments in our letter dated June 22, 2011 and have the following additional comments. All page numbers below correspond to the marked version of your filing.

General

1. We note your response to our prior comment one. Please revise throughout to provide balancing disclosure to clarify that further research of your products is needed to determine efficacy as we note that the abstracts of the reports you provided in response to our prior comment one suggest that results are preliminary and further research is needed. In addition, we note that your conclusions regarding the effectiveness of Brand B are based upon studies that utilized products other than Brand B. We also note that you have not yet completed the FDA approval process. For example, we note the fourth sentence in the second paragraph on page two, statements on pages two and elsewhere that your products do not expose users to any new side effects, the first sentence in the third paragraph on page two, the second sentence in the first paragraph on page three, the first sentence in the second paragraph on page 36, the last two sentences in the first paragraph on page 38, the last sentence of the second paragraph on page 38, the bullet points on page 39, the third sentence in the first paragraph on page 41, the third paragraph on page 41, statements in the first paragraph on page 42, the graph on page 42 and the paragraph preceding the graph, the third sentence of the third paragraph on page 42, the discussion "Clinical Trials with Cigarettes Containing our VLN Tobacco" beginning on page 43, claims regarding Rubisco in the third and fourth paragraph on page 55, and claims regarding Verfola in the fourth and fifth paragraphs on page 55.

2. In this regard, we note your disclosure in the second sentence of the "Brand A Cigarettes" section on page 41 that "[c]linical studies have demonstrated" and your disclosure on

pages 43 to 46 regarding the results of various clinical trials. Please advise as to whether the reports containing the results of these clinical trials are publicly available. If the reports are not publicly available, please provide a consent of the author under Rule 436 of the Securities Act of 1933.

Prospectus Summary, page 1

Our Company, page 1

Overview, page 1

3. Please revise to clarify your disclosure on page two and elsewhere that you believe that your VLN tobacco "does not present any new side effects." We note that it appears that the tobacco would cause many of the same side effects as smoking a non-VLN tobacco cigarette. In this regard please also note comment one above.

4. We note your response to our prior comment 25 and your disclosure on page 1 that you plan to raise approximately $15,000,000 in Fall 2011 to fund Phase III trials, modified risk exposure studies and for your general working capital requirements. Please revise to disclose here how you intend to raise such funds.

5. We note your response to our prior comments 20 and 22. Please revise the last sentence in the first paragraph of the "Overview" section on page one to indicate that you have not identified any specific countries or developed any timelines or cost estimates for international expansion.

Smoking Cessation Aids, page 3

6. Please remove the words "such as X-22" from the first sentence in this section, as The Tobacco Control Act does not specifically address your product.

Technology Platform and Intellectual Property, page 4

7. We note your response to our prior comment 16 and reissue in part. Please revise your disclosure on page 5 to clarify what you mean by your "two worldwide exclusive licenses expire upon the last-to-expire patent on a country-by-country basis, which is from 2022 through 2026."

Risk Factors, page 9

8. Please add a risk factor discussing how FDA requirements requiring graphic health warnings may impact sales of your products, as applicable. Please also revise the Government Regulation section beginning on page 51 as appropriate.

Business, page 35

Market, page 38

Cigarettes and Smoking Cessation Aids, page 38

9. Please provide a basis for statements in the first three sentences in the third paragraph and the first sentence in the fourth paragraph in this section and the second sentence in the last paragraph on page 40. Additionally, please revise to disclose the date of these statistics.

10. Please revise the second to the last paragraph on page 38 to clarify that there is no guarantee that, even if approved by the FDA, X-22 will have comparable sales to Chantix, or that the FDA will not require X-22 to have a boxed warning.

Government Regulation, page 51

Clinical Phase, page 51

11. We note your disclosure on page 52 that you have designated your upcoming phase II clinical trial as a "Phase II-B trial." Please revise to clarify whether this is your designation or if the FDA has also designated the trial as a Phase II-B trial, or please advise.

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,

/s/ John Dana Brown

John Dana Brown
Attorney-Advisor

cc: Via E-mail
Patrick G. Quick
Foley & Lardner LLP