



DIVISION OF
CORPORATION FINANCE

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

August 29, 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. 5 to Registration Statement on Form S-1
Filed August 26, 2011
File No. 333-173420**

Dear Mr. Pandolifino:

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

General

1. With a view to revised disclosure, please explain to us any reasons the FDA gave for denying fast-track designation for X-22.

Risk Factors, page 9

Risks Related to Regulatory Approvals and Insurance Reimbursement, page 14

If we fail to obtain FDA and foreign regulatory approvals of X-22, page 14

2. We note your disclosure on page 14 that "if you are not able to have X-22 qualify for Fast Track designation by the FDA, [you] will not receive the benefit of a priority review from the FDA" on page 14. Please expand this risk factor to disclose that you "previously submitted a request for Fast Track designation and on August 18, 2011, the FDA informed [you] that designation of X-22 as a Fast Tract Product [could not] be granted at this time, but, if [you] desire further consideration, [you] should submit a new request for Fast Track designation."
3. Please revise to provide a separate risk factor addressing how your business will be impacted if you are unable to receive Fast Track designation and a priority review of X-22 from the FDA, including what the effects may be on the timing and costs of obtaining

Joseph Pandolifino
22nd Century Group, Inc.
August 29, 2011
Page 2

FDA approval for X-2 and its impact on your financial condition. This disclosure will help investors better understand this risk.

Principal and Selling Shareholders, page 28

Selling Shareholders' Table, page 29

4. Please revise footnote 14 to identify the individual or individuals who have voting or investment power with respect to the shares held by Gibralt US, Inc.

Management's Discussion and Analysis of Financial Condition and Results of Operation, page 58

5. We note your revision to the first sentence in the third paragraph of this section. Please delete this sentence as this is not a quarterly report. We also note that the PSLRA safe harbor for forward-looking statements in Section 27A of the Securities Act is not applicable to you.
6. We note your response to our prior comment two and reissue in part. Please revise to include disclosure regarding the annual "clean-up" provision that requires you to repay all principal amounts outstanding and disclosure that you have not complied with the "clean-up" provision. In addition, please revise to add a risk factor that addresses your failure to comply with the "clean-up" provision or tell us why this is not necessary.
7. We note your revision on page F-28 regarding the promissory note dated June 30, 2011 that is due on August 30, 2011. Please revise to add disclosure here regarding this note or advise.

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