TITLE: Product Complaints System
PRODUCT: VLN™ Kings and VLN™ Menthol Kings
STUDY No.: <to be determined>

Background:	22nd Century Group, Inc. ("22nd Century") is planning to introduce VLN™ cigarettes to the US market that are anticipated to have a positive safety profile in comparison to other cigarettes containing a higher level of nicotine. With anticipated significant user exposure to this new cigarette product, 22nd Century plans to initiate a product complaint system that allows collection of post-marketing safety data to confirm the anticipated safety profile.
Safety Data Collection:	A dedicated telephone number and email address for reporting of product complaints will be implemented and published on 22nd Century's website and on promotional material relating to 22nd Century's products, e.g. press releases, advertisements in newspapers and magazines, internet advertisements, etc. In addition, 22nd Century's employees will receive training on the recognition of product complaints and will be required to forward to the dedicated contact information any product complaints they become aware of during discussions with users or healthcare professionals. Any vendors or commercial partners also will be required to forward product complaints, with such requirements included into their contracts with 22nd Century. The telephone number and email address will be monitored during routine business hours in the Eastern Time Zone, with the telephone number providing voicemail facilities out of hours. Users and healthcare professionals will be able to report any product complaints, safety concerns or 'adverse experiences' via these contact information pathways. The monitoring will be performed by an experienced team of information professionals accustomed to collecting adverse experience reports for a wide range of products across the pharmaceutical industry. Reporters will be questioned to determine all available information about each user's experience, including important comorbidities. All calls and emails received will be entered into an information database and assessed by an experienced member of staff to see if they contain an adverse experience (i.e. an adverse event as defined by ICH E2D). Each adverse experience will be entered into a safety database and reviewed by a safety physician. The safety physician will determine if additional information is required to understand the user's experience and follow-up information will be requested from the reporter to build a robust database of information about the VLN™ cigarettes. Reconciliation between the information database and safety database will be performed at regular intervals to ensure that all adverse experiences have been appropriately identified and transferred to the safety database.
Safety Data Reporting:	Each adverse experience report will be assessed to determine if there is a potential relationship between the symptoms experienced by the user and the VLN™ cigarettes. If the reporter considers there is a relationship, a positive causality will be assumed by 22nd Century. If the reporter does not provide an opinion or considers there is no relationship, a further assessment of causality will be made by the safety physician involved in the processing of the adverse experience in the safety database. If either the reporter or the safety physician considers there is a possibility that VLN™ cigarettes caused the user's symptoms, or there is insufficient information to make a conclusion about a relationship, a report about the user will be submitted to the US Food and Drug Administration (FDA). Reports will be submitted as ICH E2B electronic reports via the FDA's Safety Reporting Portal as follows: - Adverse experiences that meet ICH E2D criteria for 'serious' will be submitted

	within 15 calendar days of receipt as expedited safety reports; - Adverse experiences that do not meet the above criteria (i.e. are 'non-serious') will be submitted within 90 calendar days of receipt as periodic safety reports.
Safety Data Evaluation:	Trend analysis will be performed on the safety database at quarterly intervals to identify if there are emerging trends in the safety data collected. Each adverse experience term categorised as a MedDRA Preferred Term will be evaluated to determine if the reporting rate for the current quarter is more than 3 standard deviations away from the historical quarterly reporting rate for that Preferred Term, assuming that the safety data collected has a normal distribution. If a Preferred Term is more than 3 standard deviations from the historical reporting rate, a potential safety issue will be highlighted and investigated. The data will be reviewed by a Safety Committee that includes professionals accustomed to evaluating safety data. If an emerging trend or potential safety issue is identified, an action plan will be agreed that may include one or more of the following actions depending on the nature of the trend identified: - No action when safety data conforms with the current understanding of the safety profile of VLN™ cigarettes or is confounded by other factors that create a statistical abnormality; - Continued monitoring to see if future data received confirms or refutes the trend; - Development of a communication plan for users and/or healthcare professionals; - Updates to published information for the VLN™ cigarettes; - Discussions with the FDA regarding suitable actions; - Changes to the legal/registered status of the VLN™ cigarette.