Roles and Responsibilities Appendix

		Canada	
		NCIC -CTG	Company
1	**PROTOCOL**		
1.1	Protocol preparation		
1.2	Protocol review		
1.3	Protocol distribution to the centres		
1.4	Preparation of Country specific appendices		
2	**PROTOCOL AMENDMENTS**		
2.1	Amendment preparation		
2.2	Amendment review		
2.3	Amendment distribution to the centres		
2.4	Checking REB approvals prior to amendment implementation		
2.6	Tracking approvals		
3	**CASE REPORT FORMS (CRFs)**		
3.1	EDC database/CRF design		
3.2	EDC database/CRF template review		
4	**CONSENT (IC) FORM**		
4.1	IC sample preparation, review and approval		
4.2	IC translation to French/Other		
4.3	Review and approval of changes in the local ICs		
5	**SERIOUS ADVERSE EVENT (SAE) REPORTING**		
5.1	Forwarding SAEs to Company (state frequency)		
5.2	Forwarding protocol-reportable SAEs from Canada to Company		
5.3	CTG to notify Company of all SAE's reported to regulatory authorities		
5.4	All queries from the Company regarding SAEs to be routed via NCIC CTG		
6	**CONTACT WITH HEALTH AUTHORITIES (HA)[0]**		
6.1	Submission of all necessary documentation to the HA, including protocol amendments		
6.2	Submission of annual reports to HA as required		
6.3	Annual meeting book summary (pooled safety data) to the Company		
6.4	Reporting of regulatory-reportable SAEs (SL) to HA		
6.5	Reporting of regulatory-reportable SAEs from other IL21 trials (ISL's) to NCIC CTG		
6.6	Forwarding SL's and ISL's to centres		
6.7	Forwarding updated IB's to centres		
6.8	Tracking proof of submissions of SL's/ISL's to REBs		
7	**MEDICINAL PRODUCT (MP)/STUDY DRUG**		
7.1	Manufacturing Packaging/Labeling and release (1º)		
7.2	Import License		
7.3	Review of label compliance with regulations		
7.4	Shipping / Distribution to centres (initial shipment and re-supply made upon receipt of IPRF)		
7.5	Provision of shipping receipts to NCIC CTG		
7.7	MP Recall		
7.8	Destruction of unused MP		

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7.9	MP reconciliation and accountability		
8	**REB / ETHICS ACTIVITIES**		
8.1	Forwarding regulatory-reportable SAEs and Safety Updates to centres		
8.2	Provide Product Monograph, Investigator Brochure and updates to NCIC CTG in electronic format for posting on website[1]		
8.3	Tracking proof of submission of safety letters (SL)/safety updates (ISLs) to REBs		
8.4	Checking REB approval of protocol/amendments		
8.5	REB fees if applicable (NA, included in site per case funding)		
9	**SELECTION OF INVESTIGATORS**		
9.1	Selection of Investigators		
9.2	Release of authorized centres list		
9.3	Termination of centres		
9.4	Assurance that sites work according to GCP		
10	**AUDITING AND MONITORING**		
10.1	Central Monitoring (i.e. off-site monitoring in the NCIC CTG office utilizing copies of source data per NCIC CTG standard)		
10.2	Auditing Plan Per NCIC CTG Standard		
10.3	Centre Audits/Monitoring		
10.4	Pre NDA audits		
11	**TRIAL/CENTRE INITIATION**		
11.1	Participating Centre Agreement		
11.2	Checking of documentation necessary for centre activation		
11.3	Formally activating a centre and completion of the Investigational Product Release Form (IPRF)		
12	**INVESTIGATOR MEETINGS / TRAINING**		
12.1	Study review at annual NCIC CTG Spring Meeting		
12.2	Planning and conducting investigator meetings		
12.3	Costs of meetings		
13	**DATA MANAGEMENT**		
13.1	Data management plan		
13.2	Review of the data management plan		
13.3	Statistical analysis plan		
13.4	Review of the statistical analysis plan		
13.5	Initial patient registration and randomization		
13.6	Timely data submission from centres		
13.7	Updating database, data checking		
13.8	Cross checks of database		
13.9	Final clinical validation of cases		
13.10	Data Queries generation		
13.11	Timely Data Query resolution		
13.12	All data queries from Company (including SAE queries) will be routed via CTG		
13.13	Coding and cleaning of concomitant medication database		
13.14	Interim data transfer (specify type and frequency)		
13.15	Database provision to the Company as SAS datasets (state timing); test database will be provided prior to this to allow writing of "transfer programs" at an agreed time, if requesting		

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13.16	MEDRA Coding of adverse events (MEDRA mapping for CTCAE supplied by CTG)		
14	**TRIAL CLOSE OUT**		
14.1	Decision on appropriate time for closure according to number of patients required.		
14.2	NCIC CTG will inform Company, and Investigators of trial closure		
15	**OTHER STUDY RELATED ACTIVITIES**		
15.1	Retention of CRFs		
15.2	Retention of regulatory files		
15.3	Writing of Investigator Brochure/addendums		
15.4	Setting up the randomization system		
15.5	Reviewing and checking the randomization system		
16	**SAFETY MONITORING**		
16.1	Internal NCIC CTG safety monitoring and IC update		
16.2	Forward relevant clinical and preclinical information to NCIC CTG		
17	**COMMUNICATION**		
17.1	NCIC CTG should receive an advance copy of all communications sent to the investigators by the Company		
17.2	Primary contact with centre		
17.3	Company to be copied on all global trial communications		
17.4	Regular conference calls		
17.5	Costs of any courier / faxes not part of NCIC CTG SOP		
18	**STATISTICAL ANALYSIS AND TRIAL REPORT**		
18.1	Analyses for CTG Spring Meeting books and final analyses		
18.2	Preparation of final report and all primary publications		
18.3	Review of final report and publications		
18.4	Preparation of Company's final study report (for regulatory filing etc.)		
19	**MISCELLANEOUS**		
19.1	Retrieval of archival tissue for Tumour Banking		
19.2	Housing of banked tissue and maintaining the tissue bank		
19.3	Cost of shipping and analyses for all samples		
19.4	Pharmacokinetic and immunogenicity studies		
19.5	Vendor for research laboratory studies		
19.6	Vendor for central review of imaging studies		
19.7	Provision of final results of laboratory analyses (state timing)		
19.9	Obtaining and maintaining Financial Disclosure Information from Investigator if required		