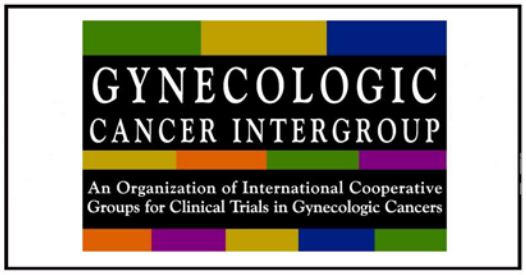

HARMONIZATION WORKING GROUP

GROUP AUDIT SUMMARIES
NOV 2013

AGO-AUST	
Monitoring	external monitoring – trial specific contracts with CRA In some low-budget trials only inhouse monitoring done by project manager
Audit	Sponsor audits

ACRIN - pending	
Monitoring	
Audit	

AGO Study Group(Study Group of the Arbeitsgemeinschaft Gynaekologische Onkologie)	
Monitoring	Usually there is an onsite monitoring conducted by a preferred monitoring company (CRO). Intervals for monitoring visits are defined in the monitoring plan and depend on the accrual rate at the local site. Tasks monitoring: • Source data verification depending on monitoring plan • Verify site's compliance with regulations/requirements • Study drug accountability A monitoring report will be send to the responsible project manager who reviews the report and initiates actions if necessary. In some low-budget trials there is only an in-house monitoring done by the responsible project manager.
Audit	Audits by sponsor Inspections by regional authorities planned: Audits of AGO sites by QA department

ANZGOG (Australia New Zealand Gynaecological Oncology Group)	
Monitoring	Minimum of 2 visits/site/trial where funding allows, with additional for-cause visits. Central monitoring for compliance and data quality issues.
Audit	According to Audit plans of both ANZGOG and CTC audit committees

COGi	
Monitoring	N/A
Audit	N/A

DGOG - pending	
Monitoring	
Audit	

EORTC (European Organisation for Research and Treatment of Cancer)	
Monitoring	Limited capacity in house, need for a CRO for extensive monitoring
Audit	Systematic audits every 3 years for biggest recruiters, case by case on-purpose audits for other sites

GEICO (The Grupo Español de Investigación en Cáncer de Ovario)	
Monitoring	GEICO use to contract a CRO for protocol monitoring. Monitoring may be on site or by phone depending on fundings.
Audit	Audits – Depending on protocol and funding.

GICOM - pending	
Monitoring	Depending on the protocol specific schedule, recruitment and funding. An external local CRA is hired by GICOM for performing this task
Audit	According to the Protocol development at the site, usually every two years or before if required. GICOM PM performs QC visits minimun2 visits/site/trial/year

GINECO (Group d'Investigateurs Nationaux pour l'Etude des Cancers Ovariens)	
Monitoring	*Internal CRAs for national studies – For international studies or big studies, use of a CRO*
Audit	Internal Quality assurance department – internal audits (SOPs, TMF…) and sometimes on site audits. Audits from sponsor when Pharma Industry – Inspection from French CA

GOG (Gynecologic Oncology Group)	
Monitoring	Study data are individually monitored by the clinical data coordinator, study chair, and study statistician. A statistical report of active and maturing studies is prepared semiannually which is distributed group-wide at each GOG group meeting for discussion by the responsible committee(s). Study accrual is monitored quarterly by the Protocol Committee. On a semiannual basis, the DSMB monitors toxicity and the DMC reviews all interim analyses of phase III studies. Institutional membership requirements are reviewed at each semiannual meeting.
Audit	New parent (main member) institutions are audited within 18 months of their first patient entry. Affiliate and subsequent audits are conducted at least once every 36 months in compliance with the NCI Clinical Trials Monitoring Board (CTMB). A minimum of 10% of the therapeutic cases are audited. The audit program is coordinated by the SDC and administered by the Group Audit Committee. All audits are submitted to the NCI utilizing the CTMB-AIS (Automated Information System). Unacceptable audits require an 18-month re-audit.

GOTIC - pending	
Monitoring	
Audit	

ICORG (All Ireland Cooperative Oncology Research Group)	
Monitoring	Central monitoring is performed by the ICORG Group Central Office according to the rules specified in protocol. Study accrual is monitored quarterly at the DSSG meeting. Review by a Data and Safety Monitoring Board (DSMB) if applicable
Audit	Conducted by the ICORG Quality & Training Manager internally and also by external sponsors.

JGOG (Japanese Gynecologic Oncology Group)	
Monitoring	Protocols dependent. For the group-wide protocol, the central monitoring will be performed by the Kitasato Data Center according to the rules specified in protocol. For all indication-directed clinical trials, as well as some trials under the newly developed regulatory system called Evaluation System for Advanced Medical Care, site monitoring including SDV is performed. For the developmental therapeutic protocol sponsored by pharmaceutical companies, the on-site monitoring may be performed by CRO that has a contract with the pharmaceutical company
Audit	Protocol dependent. For the group-wide protocol the audit will be performed by the members of protocol-specific audit committee. For the developmental therapeutic studies sponsored by pharmaceutical companies, the participating institutions are subject of audit by Japanese Government as well as audit teamd from the sponsor.

KGOG (Korean Gynecological Oncology Group)	
Monitoring	Conducted on trials which require on site monitoring by the RA. Extensive study validation programs written for each study used to verify data and helps generate queries. Some data goes through a visual review by an RA. Study is monitored for timing of interim efficacy and/or other possible early stopping rule analyses and final analyses.
Audit	Once the trial is underway the KGOG may wish to carry out random audits of individual studies.

MaNGO - pending	
Monitoring	
Audit	

MITO (Multicenter Italian Trials in Ovarian cancer and gynecologic malignancies group)	
Monitoring	Each clinical trial has a monitoring plan in the protocol, and the level of monitoring is based on risk. All trials have centralized monitoring. On-site monitoring may be planned, and may be carried out by the coordinating center or by a CRO.
Audit	Systematic audit plan for MITO centers is under development. Internal audit may be conducted at coordinating center (Institution), and regular or for cause auditing may occur at recruiting centers.

National Cancer Research Institute UK (NCRI) and Medical Research Council (MRC) CTU /UCL CTC	
Monitoring	Decisions on the type and frequency of monitoring for a trial are risk-based. The CTU involved will develop a trial monitoring plan for each trial. Monitoring usually involves a mixture of on-site and central monitoring methods. Monitoring activities are undertaken by CTU staff, third party contractors or for a GCIG trial may be delegated to another GCIG group to undertake within their country.
Audit	CTUs are subject to regulatory inspection, sponsor audit, and have internal audit/review systems in place. Audits of trial sites and third party suppliers etc may be undertaken by the CTUs if indicated, based on risk.

NCIC CTG (NCIC Clinical Trials Group)	
Monitoring	The NCIC CTG Central Office contains a large Audit and Monitoring Group (AMG) that performs on site monitoring (OSM) for Canadian institutions. The OSM program has 3 main programs: On-site Monitoring Canada: Standard Monitoring Program (OSM-C), On-Site Monitoring International (OSM-I), and On-Site Monitoring Residual (OSM-R). **On-Site Monitoring Canada: Standard Monitoring Program** The OSM-C or standard program applies to the majority of NCIC CTG trials. As part of this program, the Audit and Monitoring Group (AMG) will select centres for monitoring as part OSM-C standard monitoring program. The selection of centres and timing of the monitoring visits will be based on but is not limited to the following: • New centres within 18 months of initial accrual • Other centres a minimum once every 36 months • Phase I/II IND centres and high accruing centres will be visited annually Centres of concern as flagged by previous monitoring/auditing findings trial team following central monitoring, may be visited more frequently. In addition to centre and frequency requirements, trial complexity or risk are factored into review requirements at each centre. Aspects considered include but are not limited to enrolment, agents under CTA or US IND, safety issues, and trial complexity. Further, if an unacceptable rating has been assigned in one or more categories of review, the next monitoring visit will be conducted within 12 months of the non-compliant visit. The follow up visit will be conducted either on site or by fax depending on nature of the issues noted.

	During on site review patient, pharmacy, ethics, essential documents, and standard operating procedures are reviewed. A minimum of 10% of patient cases per trial per centre is selected for review depending on the criteria and/or issues noted. With respect to patient review, source data verification and protocol compliance assessment is conducted on informed consent, eligibility, baseline, treatment, follow up, SAE, and endpoint information for cases selected. **<u>On-site Monitoring International (OSM-I)</u>** The OSM-I or International program utilized similar principles as described for OSM-C but it applies to single study centres in the United States. These centres participate directly through NCIC CTG. Where no other audit and monitoring oversight is in place, NCIC CTG will conduct audit and monitoring. **<u>On-site Monitoring Residual (OSM-R)</u>** The OSM-R residual or intensive monitoring program is similar to an industry model where centres are visited every 6-8 weeks and up to 100% source data verification is completed. Separate contracts and budgets are in place for this type of monitoring. Generally this is performed for NDA trials.
Audit	The NCIC CTG audit program includes on site audits of trials, vendors, and internal audits of NCIC CTG trials and associated processes. With respect to on site audits of trials, audits are conducted at participating centres for Phase III trials for which NCIC CTG is the sponsor which includes trials which are monitored by a pharmaceutical company or contract research organization (CRO). Other trials (phase I or II trials, or trials for which NCIC CTG is not the sponsor) may be selected for audit as part of a routine program or based on prior monitoring/auditing findings of concern. In general, audits are conducted at Canadian centres, but audits of international centres may also be conducted for selected trials. **Centre Selection** Once the trials to be audited are identified, AMG will select centres for audit. The selection of centres will be based on but not limited to the following: • Centre enrolment, with emphasis toward high enrolling centres. • Centre workload. • Centres using a new investigator, new staff, or new systems. • Co-coordinating investigator centres. • Centres considered of concern based on central or prior monitoring/auditing.
NOGGO (North-Eastern-German Society of Gynaecological Oncology)	
Monitoring	Protocol dependent. Usually the cooperating CRO conducts the monitoring defined by the monitoring plan. Tasks monitoring: • Source data verification depending on monitoring plan • Verify site's compliance with regulations/requirements • Study drug accountability A monitoring report will be send to the responsible project manager who reviews

	the report and initiates actions if necessary.
Audit	Audits by sponsor. Inspections by regional authorities

NSGO (Nordic Society of Gynaecological Oncology)	
Monitoring	Trial specific
Audit	Trial specific
PMHC (Princess Margaret Consortium)	
Monitoring	A formal data management and monitoring plan is developed for each trial in which PMHC is the lead. All quality control monitoring utilizes a targeted approach based on risk. Data is entered by sites directly into the database using guidelines developed by PMH. Training of staff will be required at all levels to ensure understanding of tasks. A formal data management plan will be in place for the PMHC studies. The study coordinators in DDP will receive the data and perform data management activities. Queries will be produced electronically and can be efficiently tracked and managed. Data will be cleaned prior to final analysis. Quality control procedures will be in place as outlined by the data management / monitoring plan developed for each trial, as stated above. Onsite monitoring will validate the e-CRF against the source data. There is a Data and Safety Monitoring Board (DSMB) for all clinical trials run by the PMHC. The Board consists of three experts in the area of the study diseases and the members are completely unrelated to any clinical trials. The statistician provides the Board all safety data and the Board convenes regularly and reviews the progress of all trials.
Audit	A formal auditing plan will be developed for trials lead by PMHC through the GCIC. It will take into account specific quality control measures that will be reviewed: i) On-site monitoring to perform checks on source data to confirm congruency with the data collected in the electronic CRFs ; ii) Reviewing staff adherence to data management SOPs; and iii) Cross checking training records to online training, site delegation lists.

RTOG (Radiation Therapy Oncology Group)	
Monitoring	Study is monitored by the RA, statistician and dosimetrist. Extensive study validation programs written for each study used to verify data and helps generate queries. Some data also goes through a visual review by an RA. Study is monitored for timing of interim efficacy and/or other possible early stopping rule analyses and final analyses.
Audit	All member facilities are audited once every three years with all facilities at risk yearly. New full member institutions are audited within 18 months of becoming full members. New affiliate members are audited within 18-36 months based on patient accrual.

SGCTG (Scottish Gynaecological Cancer Trials Group)	
Monitoring	On site monitoring performed by CTU monitoring team, level of on site monitoring performed determined by risk assessment of each trial and monitoring budget available for trial. Central monitoring performed to check for compliance with protocol, data consistency, missing data and timing.
Audit	According to audit plans of CTU. In addition studies may be subject to inspection and audit by study sponsor and other regulatory bodies i.e. MHRA to ensure adherence to GCP.

SGOG (Shanghai Gynecologic Oncology Group)	
Monitoring	Each clinical trial is monitored by the data managers and site chair in local site. And they are overviewed by the executive committee once every two weeks.
Audit	Systematic audit plan for SGOG is under development. Two ongoing clinical trials of SGOG are audited by Local Ethics committee.