Quality Control for Phase 1 Trials – Site Perspectives

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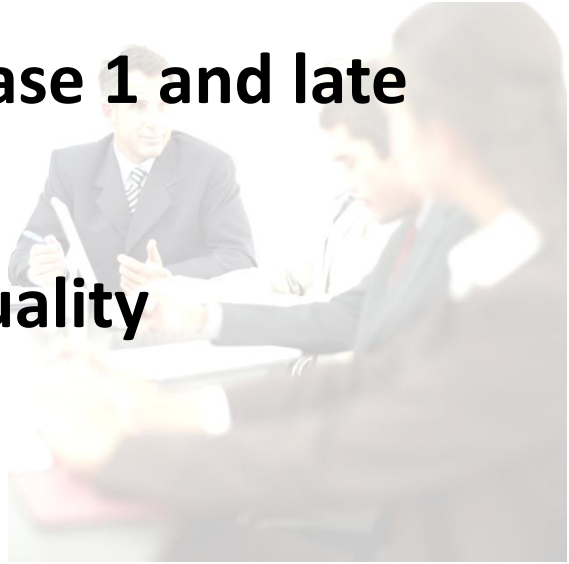
Changi General Hospital

Presentation Overview

1. What is QC?
2. What is Phase 1 Trial?
3. What are the Differences between Phase 1 and late Phase Requirements for QC?
4. What to take into consideration for Quality Improvement?
5. Take Home Message



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Quality control is a process by which entities review the quality of all factors involved in production.

Wikipedia, the free encyclopedia

QC is the real time, on-going (day-to-day) operational techniques and activities that are undertaken to verify the requirements for quality trial-related activities.

National Institutes of Health

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Why Site need to do QC?

- Effective protocol implementation
- Assure compliance with GCP, Sponsor and applicable regulatory requirements
- Assure correct Timing of trial tasks
- Verify data accuracy
- Avoid protocol deviation
- Avoid Harm to Subjects
- Assure Trial integrity
- Identify areas in need of corrective action
- Assure a constant state of readiness for an external audit or monitoring visit

Phase	Number and type of subject	Questions
1	50-200 **healthy subjects** (*usually*) or **patients** who are not expected to benefit from the IMP	• Is the IMP safe in humans? • What does the body do to the IMP? (*pharmacokinetics*) • What does the IMP do to the body? (*pharmacodynamics*) • Might the IMP work in patients?
2	100-400 **patients with the target disease**	• Is the IMP safe in patients? • Does the IMP seem to work in patients? (*efficacy*)
3	1000-5000 **patients with the target disease**	• Is the IMP really safe in patients? • Does the IMP really work in patients?
4	many thousands or millions **patients with the target disease**	• Just how safe is the new medicine? (*pharmacovigilance*) • How does the new medicine compare with similar medicines?

Reference From Association of the British Pharmaceutical Association 2007

Healthy Subjects

Eeasier to find

Free of other medicine

More likely to respond uniformly

Better at completing long and complex trials.

Tolerate IMPs better

Patients with Target Disease

Cytotoxic drug

Gene therapy

The Quality depends a lot on how the Site conducts the Study.

Sponsor

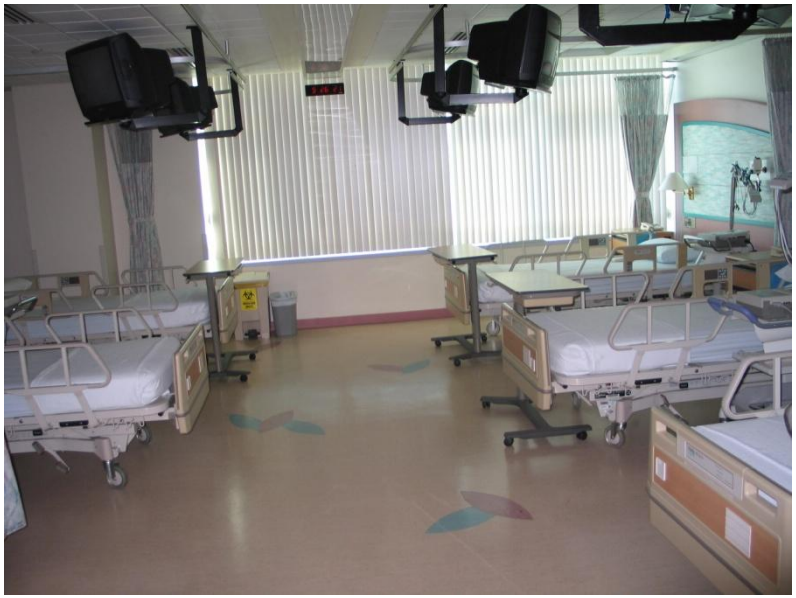
Feasibility

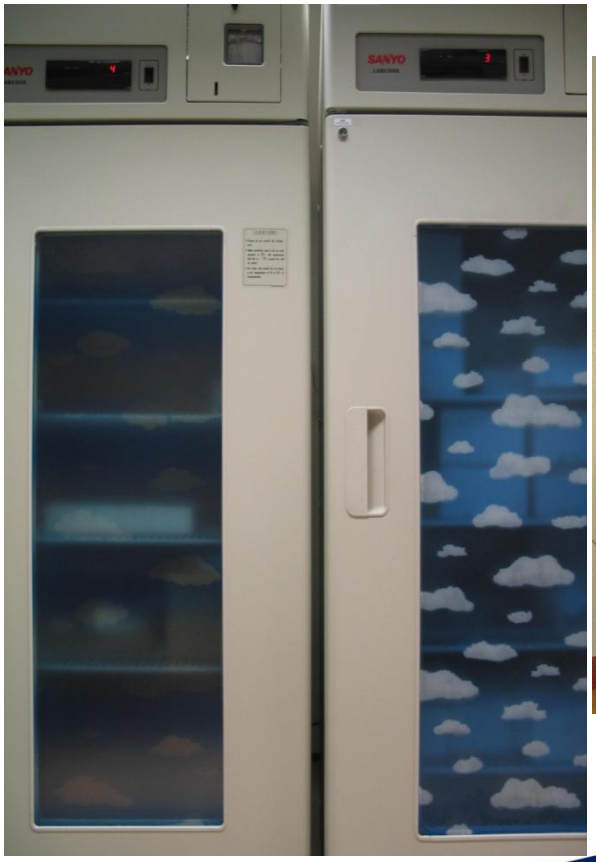
Pre-study audit

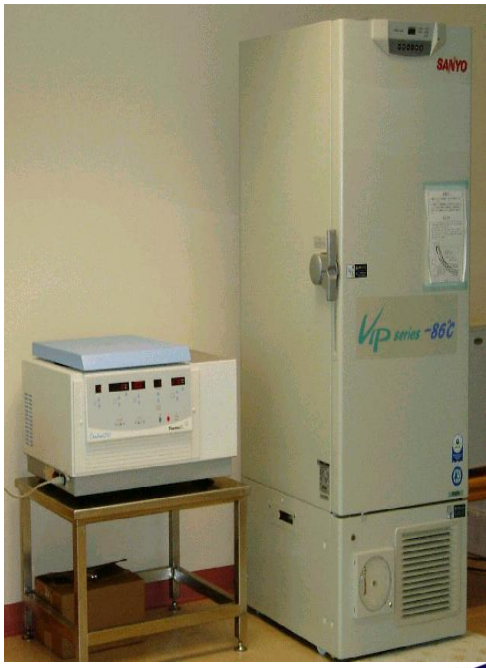
Site

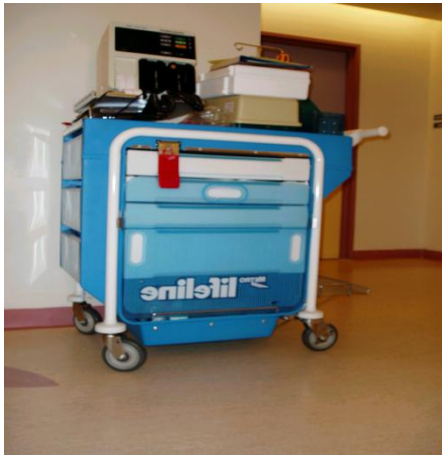
Plan based on the design and complexity of the study protocol and data to be collected

Prepare and check each stage of the trial to ensure applicable standards are followed and that the data generated are correct.









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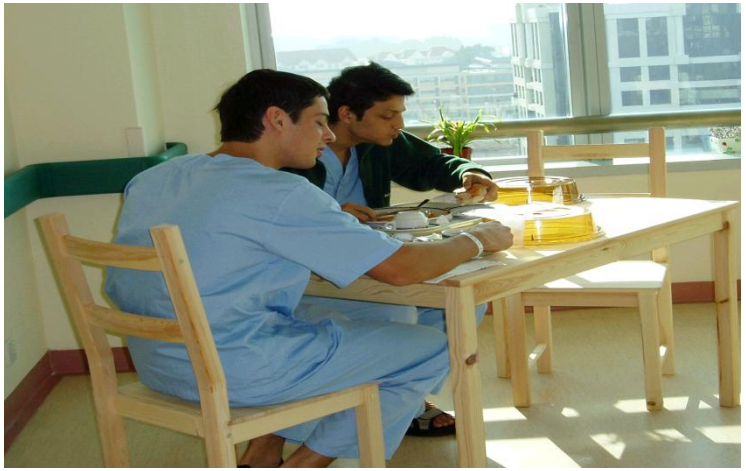

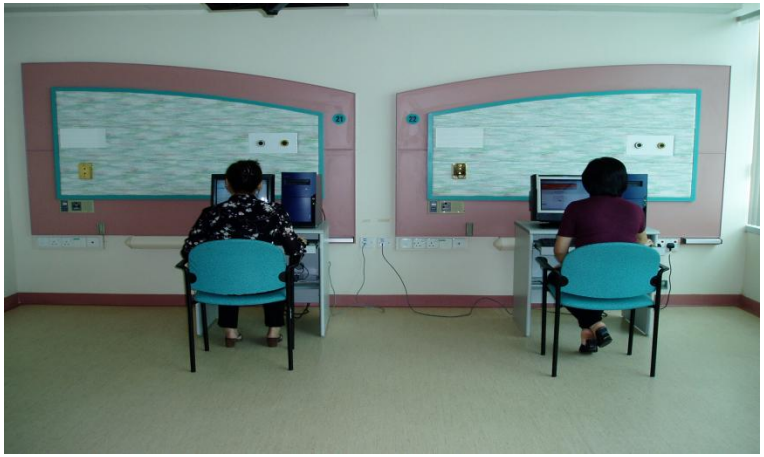

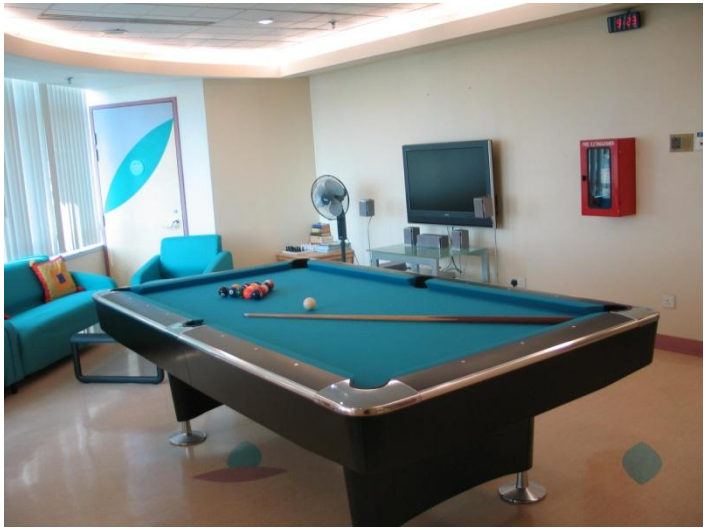

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TempTrak Current Sensor Readings

CTRU

☐ Show Only Out-of-Range Sensors
☐ Use Dial Display
☐ Show Group Audit Charts

All Group Summary | REFRESH

Group: CTRU Freezer

Freezer 1 (40004016)	Freezer 2 (42000031)	Freezer 3 (828434-6106)
TEMPERATURE	TEMPERATURE	TEMPERATURE
-78.6°C	-81.0°C	-79.7°C
Range: -81.0°C - -60.0°C	Range: -81.0°C - -60.0°C	Range: -81.0°C - -60.0°C
25/7/2013 11:00:00 AM	25/7/2013 11:00:00 AM	25/7/2013 11:00:00 AM
Sensor ID: 238-152/E	Sensor ID: 238-90/E	Sensor ID: 178-172/E

Group: CTRU Fridge

Drug 1 (40004361)	Drug 2 (42000051)	Urine Fridge (42000066)
TEMPERATURE	TEMPERATURE	TEMPERATURE
3.4°C	3.4°C	4.5°C
Range: 2.0°C - 8.0°C	Range: 2.0°C - 8.0°C	Range: 2.0°C - 8.0°C
25/7/2013 11:00:00 AM	25/7/2013 11:00:00 AM	25/7/2013 11:00:00 AM
Sensor ID: 237-239/E	Sensor ID: 238-75/E	Sensor ID: 238-120/E

Group: CTRU IMP Room

IMP Room Temperature
TEMPERATURE
22.3°C
Range: 20.0°C - 25.0°C
25/7/2013 11:00:00 AM
Sensor ID: 237-210/E

Medical Coverage?

Available at Dosing
Hospital Medical emergency & code-blue

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Sufficient Manpower
-To cover all study activities
-To cover day and night shift
-To cover weekends & public holidays

Staff are qualified

Staff Training & Competency

Protocol Specific Competency Assessment

NAME OF ASSESSEE: xxx
PROTOCOL NO : xxx

PERFORMANCE STANDARD	COMPETENCY ASSESSMENT			
Vital Signs	**C**	**NYC**	**Remarks**	**Assessed By (Sign & Date)**
Verify that subject have rested in supine position for 10mins				
Verify the "Assigned arm" for BP taking				
Take BP on assigned arm, HR in supine position				
After supine measurement, instruct subject to stand upright and measure standing BP and HR immediately in standing position				
Nurse observe for sign and symptoms of fainting spell and is standing within reach of subject				
Instruct subject to remain in standing position for 2 mins				
Measure the standing BP and Heart rate at 2min timepoint				
Record time and reading into source document				

How to QC who the subject is and is the same person that attends all the visits?

How to QC subject is third generation Chinese?

What Documents to draft?
Work Allocation
Source Document
Logs

Checked against what?
Applicable Standards
Correct version of the Study Protocol
Study Manuals
CRF

Should have doc control, vetted and approved for use!

Protocol No. xxx

Work Allocation Worksheet

Date: xxx

Night Shift	Day Shift	
Staff A	Staff C	Staff G
Staff B	Staff D	Staff H
	Staff E	Staff I
	Staff F	Staff J

Task : Day 1	1001	1002	1003	1004	1005	1006
Predose Supine Vital signs (BP, PR, Temp)	7:05	7:10	7:15	7:20	7:25	7:30
Predose 12 Lead ECG	**7:10**	**7:15**	**7:20**	**7:25**	**7:30**	**7:35**
Final eligibility review	7:15	7:20	7:25	7:30	7:35	7:40
Predose PK blood collection (5mls), ice bath	7:25	7:30	7:35	7:40	7:45	7:50
Breakfast	7:30	7:35	7:40	7:45	7:50	7:55
Dosing of study drug with 240mls water	**8:00**	**8:05**	**8:10**	**8:15**	**8:20**	**8:25**
0.5hr AE & Conmed check	8:15	8:20	8:25	8:30	8:35	8:40
Instruct subject supine for 10mins	8:15	8:20	8:25	8:30	8:35	8:40
0.5hr Supine Vital signs (BP, PR, Temp)	8:20	8:25	8:30	8:35	8:40	8:45
0.5hr 12 Lead ECG	**8:25**	**8:30**	**8:35**	**8:40**	**8:45**	**8:50**
0.5hr PK blood collection	8:30	8:35	8:40	8:45	8:50	8:55
1hr AE & Conmed check	8:45	8:50	8:55	9:00	9:05	9:10
1hr Supine Vital signs (BP, PR, Temp)	8:50	8:55	9:00	9:05	9:10	9:15
1hr 12 Lead ECG	8:55	9:00	9:05	9:10	9:15	9:20

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Screening No.	S	C	R			
Randomisation No.						
Date						

dd mm yyyy

Subject Initials			

Day 1 (MAD)

Study Drug Administration (Please tick (✓) the appropriate box)

Check that subject has fasted at least 10 hours prior to administration of study medication, except water up to 1 hour prior to study drug administration.

Dosing Instructions to subject:

- Study drug to be taken orally with **240 mL** of room temperature water in upright position.
- Study drug to be swallowed whole and not chewed, dissolved or crushed.
- No food until 4 hours after dosing, no water until 1 hour after dosing.

Study Drug	Dosing Time <24 hr clock>	Compliance check	Done by	Verified by
XXX ___ mg / Placebo	__ __ : __ __	☐ Dose with 240ml water ☐ Hand and Mouth check		

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Screening No.	S	C	R			
Randomisation No.						
Date						

dd mm yyyy

Subject Initials			

Day 1 (MAD)

PK Collection

Time Point	Collection Time <24 hr clock>	Comment (if any)	Staff's Initial
Post dose 30 min	__ __ : __ __		
Post dose 1 hr	__ __ : __ __		
Post dose 2 hr	__ __ : __ __		
Post dose 3 hr	__ __ : __ __		
Post dose 4 hr	__ __ : __ __		

Subject Initials: | | | |

Screening No.: | | | | | |

Randomization No: R N R | | |

PK Sample Processing Log

Protocol Day (date)	Time Points	Time Into Centrifuge	Comments (if haemolysed, indicate degree)		Time Into -70^{0}CFreezer	Remark	Staff's Initial
Day 0 (__/__/____)	Pre-dose	:		Slightly	:		
				Moderately			
				Severely			
	0.25 hr Post-dose	:		Slightly	:		
				Moderately			
				Severely			
	0.5 hr Post-dose	:		Slightly	:		
				Moderately			
				Severely			
	0.75 hr Post-dose	:		Slightly	:		
				Moderately			
				Severely			
	1.0 hr Post-dose	:		Slightly	:		
				Moderately			
				Severely			
	1.5 hr Post-dose	:		Slightly	:		
				Moderately			
				Severely			

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Importance of maintaining clinical trial quality and keeping accurate records throughout the life--cycle of a clinical trial for

Decision making by stakeholders
Dose escalation?
Stopping the trial?
Proceed/discontinue with the IP development?
To use the Site again?

Advice to CRCs

Be Aware of your role & responsibility
Learn from mistakes
Learn from the audits and inspections
Learn the Corrective & Preventive Actions
Refer to the relevant Documents
Be resourceful, Consult when in doubts
Communicate proactively
Identify and highlight problems and concerns early

Deming's PDCA cycle

Plan: The plan to retrain the persons who have committed the error

Do: Do the planned changes. Retrain the persons who have committed the error

Check: to check whether the errors continue

Act: If errors disappeared, apply the plan to the whole team. If the errors persist, the cycle is repeated.

QUALITY

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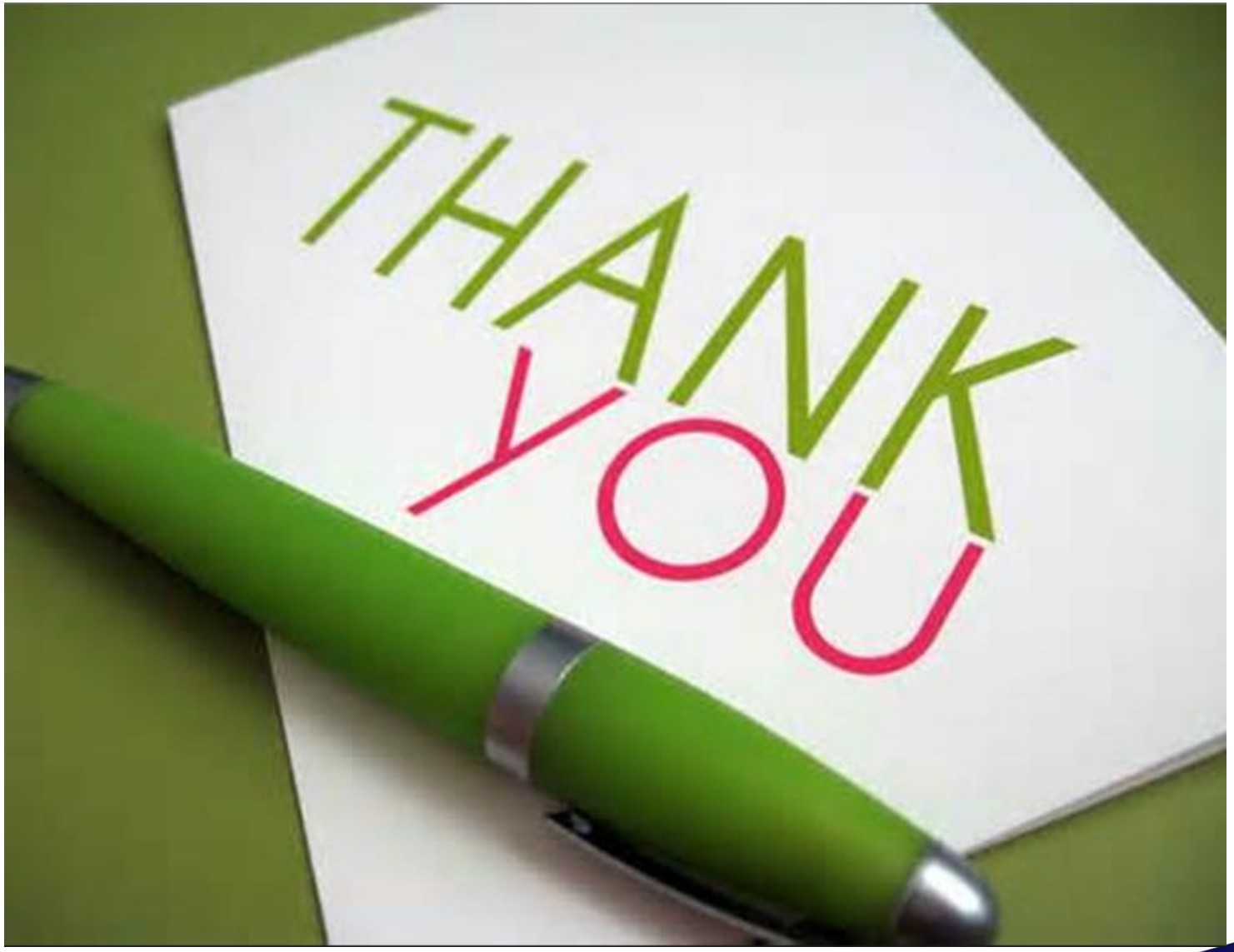

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