About Project

This project was part of an interdisciplinary learning initiative where I collaborated with fellow students from Pharmaceutical Science for a group project.

I had to conduct self-directed learning to gain context and a comprehensive understanding of the pharmaceutical tablet manufacturing process to perform my specific role of conducting data analysis to investigate issues in the manufacturing process that caused tablets to fail the British Pharmacopeia Uniformity of Weight Test and convey insights and findings using storytelling techniques.

Introduction

Kanban Pharma Ltd. Is involved in the production of three pharmaceutical products which is Mineo, Mideo, and Maxeo tablets, and as a production technician working in Kanban Pharma Ltd. involvement in the production of all three tablets is necessary. Based on the dataset provided, an analysis of trends will be conducted, and insights will be obtained. This is to ensure that the production of Maxeo tablets runs smoothly and that the tablets comply with the requirements as stated in the British Pharmacopeia and United States Pharmacopeia. The Uniformity of Weight Test will be used as a measure to ensure the quality of Maxeo tablets. Ensuring the quality and uniformity of weight of these tablets is crucial to maintain consistency for the safety and effectiveness of the medication when distributed into the market.

The Maxeo tablets are subjected to dry granulation for 8 hours where the raw material which is the active pharmaceutical ingredient is weighed and goes through screening and mixing. Compression granulation is the compaction of the components of a tablet formulation by using a flat punch and these compact masses are called a slug. This process is called slugging, and the slug goes through milling and screening to produce a granular form. Lastly, mixing and compression is done to get the finished pharmaceutical product which is the tablet.

Data Background

The dataset includes information related to the uniformity of weight of Maxeo tablets. This data is collected by randomly sampling 20 tablets at each time interval during the tablet manufacturing process.

Purpose of Analysis

The analysis aims to evaluate the uniformity of weight in Maxeo tablets and identify any factors that may contribute to variations. The goal is to maintain high-quality standards and consistency in tablet production. Manufacturing of the tablets will be stopped if tablets fail the test, and the root cause of the failure will be addressed before the manufacturing process is continued.

Business Understanding

Pharmacopeia Requirements

According to the British Pharmacopeia, if the average mass of Maxeo tablets at a particular sequence is above a certain mass, it has an acceptance criterion. According to the dataset, all the Maxeo tablets have an average mass of over 250mg. Thus, the percentage deviation acceptance criteria is 5.0% according to the *Appendix XII C. BP's Table 2.9.5-1* below. Furthermore, a requirement to pass the Uniformity of Weight Test is if not more than 2 of the individual masses of the tablets deviate by more than 5.0% and none deviate by more than twice the percentage deviation which is 10.0%.

Pharmaceutical Form	Average Mass	Percentage deviation
Tablets (uncoated and film-coated)	80 mg or less	10
	More than 80 mg and less than 250 mg	7.5
	250 mg or more	5

Appendix XII C. BP's Table 2.9.5-1

Significance of the Uniformity of Weight Test

The Uniformity of Weight Test is done to assess the quality of the tablets and to ensure consistency. If the weight of the tablet is inconsistent, the mass or amount of active pharmaceutical ingredient inside a tablet might differ from another tablet of the same batch due to weight variation. Thus, the effectiveness and consistency of the tablet cannot be guaranteed. The efficacy of the drugs may differ in each tablet and thus if released into the market may cause patients to consume tablets that has too much or too little active pharmaceutical ingredients which could lead to overdose which is fatal or an underdose. If the weight of the tablets in a batch are not consistent, the manufacturing needs to be stopped and the batch needs to be discarded and the reasons and factors that caused the failure need to be assessed to ensure that it does not occur again during sampling of the next batch.

Factors Affecting Uniformity of Weight

When manufacturing tablets there are many different steps done as shown in the methodology of the tablets below and in these steps, there could be certain factors that could affect the uniformity of the tablets leading to weight variations of the tablets from the same batch.

1. **Particle Size / Size distribution**
   When the size of each granule is different, the tablet powder will have a poorer flow property. The lack of particle size uniformity would lead to poorer uniformity of weight.

2. **Poor flow properties**
   The powder flow property is the fluidity of the powder from hopper to the machine. Poor flow properties would lead to poor quality of tablet as it is a key factor to ensure tablet weight consistency. When the flow property of the powder is passable, hang up at the hopper may occur, causing powder variations in each tablet.

   According to our given dataset, our Hausner ratio is 1.34 and our compressibility index is 25%, indicating that our Maxeo tablet powder's flow characteristics is passable as seen in the United States Pharmacopeia (USP) Powder Flow Chart in *Appendix 1.1*

3. **Relative Humidity**
   A higher relative humidity leads to more damp air, increasing the moisture content in the air in the production plants of the Maxeo tablets. Thus, if at a time interval when the relative humidity is higher, it is possible that tablet could have a higher moisture content as it absorbs the moisture from the air, causing the particles to stick together. There is a decreased flowability of the tablet at a higher moisture content point.

   This may affect the powder flow properties due to moisture from high relative humidity, which will affect the filling of the die cavity during punching, which may lead to uneven filling resulting in poor uniformity of weight.

4. **Active pharmaceutical ingredient sticking to the punch tip face**
   The adhesive punch face could cause some of the Maxeo tablet powder to stick to it, pulling it away from the tablet. This will cause some powder to be lost leading to the loss in weight in some tablets. Thus, leading to poor uniformity of weight.

5. **Human Error**
   The machine such as the analytical weighing balance may be uncalibrated, thus leading to problems in weighing and amount of powder weighed could be underestimated or overestimated.

6. **Temperature**
   A variation in temperature may cause the powder in tablets, cohesive and adhesive property to be affected. This could negatively impact the flowability and filling of the die cavity, affecting the mass of each tablet which leads to a poorer uniformity of weight.

7. **Height of tablet**
   Varying heights of a Maxeo tablet may lead to varying masses of Maxeo tablets. The height of tablet directly affects the weight of tablet. If the height of a tablet is different from another tablet, its weight of powder will then differ. This will lead to poor uniformity of weight of Maxeo tablets.

Methodology

1. Conduct random sampling on the batch by picking 20 tablets from the batch
2. Weigh each of the tablets and record the mass at 15 minutes
3. Replace the 20 tablets after each 15 minutes intervals with another 20 tablets from the batch
4. Calculate the average weight of the 20 tablets after each time interval
5. Find the percent deviation of each of the tablets at each time interval using this formula:
$$\frac{|average - mass|}{average} \times 100\%$$
6. Determine if each tablet passes or fails the Uniformity of Weight Test using the percent deviation acceptance criteria in the British Pharmacopeia in *Appendix 1.1*
7. Determine if each time interval fails and if the batch of Maxeo tablets fail

Stakeholders of Analysis

Head of Production of Kanban Pte Ltd

The Head of Production of Kanban Pte Ltd will be the main target audience as they are responsible for overseeing tablet manufacturing and ensuring quality standards. This analysis will help them identify issues in their production of tablets and understand where they can improve in their production operations as well as reduce resource loss and profit loss due to discarding of failed batches.

Data Management

Software Used

Excel was used to split data into various datasets for analysis and conducting the British Pharmacopoeia Uniformity of Weight (Mass) Test. Tableau was used for Data Integration, where relationships were used to link various datasets using the Time column as a Common Key.

Data Quality Audit

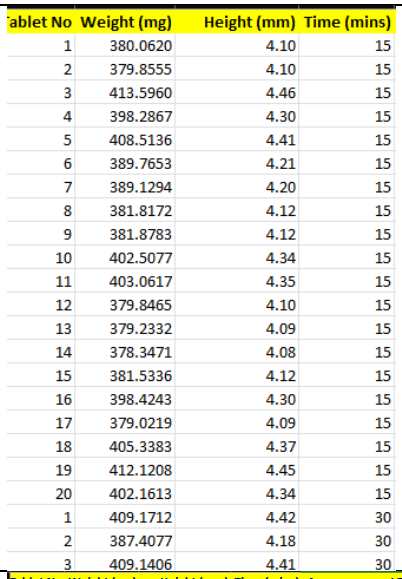
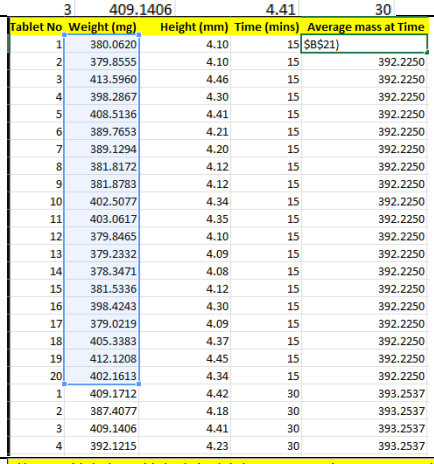
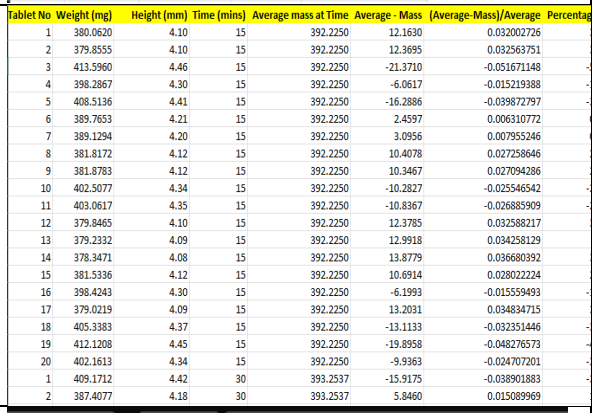
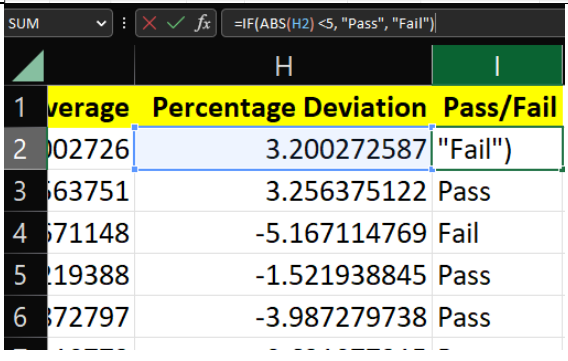
Time (min) for 8 hours	15 min		30 min		45 min		60 min		75 min		90 min		105 min		120 min		135 min		150 min		165 min		180 min		195 min		210 min		225 min		240 min	
Sequence->	[1]	[1]	[2]	[2]	[3]	[3]	[4]	[4]	[5]	[5]	[6]	[6]	[7]	[7]	[8]	[8]	[9]	[9]	[10]	[10]	[11]	[11]	[12]	[12]	[13]	[13]	[14]	[14]	[15]	[15]	[16]	
Tablet No	Weight (mg)	eight (mm)	Weight (mg)	eight (mm)	Weight (mg)	eight (mm)	Weight (mg)	eight (mm)	Weight (mg)	eight (mm)	Weight (mg)	eight (mm)	Weight (mg)	eight (mm)	Weight (mg)	eight (mm)	Weight (mg)	eight (mm)	Weight (mg)	eight (mm)	Weight (mg)	eight (mm)	Weight (mg)	eight (mm)	Weight (mg)	eight (mm)	Weight (mg)	eight (mm)	Weight (mg)	eight (mm)	Weight (mg)	eight (mm)	Weight (mg)	eight (mm)
1	390.0620	4.10	409.1712	4.42	389.9824	4.21	414.9611	4.48	393.7047	4.25	389.3965	4.20	376.1292	4.06	394.5245	4.26	414.6333	4.47	397.1549	4.29	410.5643	4.43	388.0716	4.19	377.5713	4.07	406.7636	4.39	381.0243	4.11	378.4645	
2	379.8555	4.10	387.4077	4.18	393.9843	4.25	412.2010	4.45	384.9319	4.15	392.0890	4.23	376.6231	4.06	387.5461	4.18	384.1933	4.15	390.3027	4.21	407.0660	4.39	380.8660	4.11	393.1479	4.24	401.2229	4.33	399.1057	4.31	405.6045	
3	413.5960	4.46	409.1406	4.41	411.9160	4.44	379.8806	4.10	400.5401	4.32	386.1482	4.17	403.6853	4.36	411.0057	4.43	408.3992	4.41	392.3659	4.23	411.6954	4.44	378.2189	4.08	397.7591	4.29	407.3246	4.40	377.1154	4.07	392.6026	
4	398.2867	4.30	392.1215	4.23	402.9894	4.35	413.3273	4.46	393.6346	4.25	396.3300	4.28	375.4680	4.05	382.8337	4.13	396.3995	4.28	412.6735	4.45	411.1161	4.44	390.6820	4.22	382.0933	4.12	408.8368	4.41	395.7718	4.27	383.9043	
5	408.5136	4.41	388.1150	4.19	414.7938	4.48	386.1612	4.17	406.2161	4.38	400.3085	4.32	387.3964	4.18	408.4508	4.41	414.9019	4.48	412.2717	4.45	400.7273	4.32	407.2423	4.39	381.5078	4.12	384.5505	4.15	401.0583	4.33	389.5418	
6	389.7653	4.21	384.1481	4.15	376.6886	4.06	387.3141	4.18	376.8187	4.07	395.7035	4.27	376.3375	4.06	400.4808	4.32	377.7049	4.08	387.1601	4.18	413.9104	4.47	385.0590	4.15	410.4544	4.43	392.4518	4.23	409.2823	4.42	383.2970	
7	389.1294	4.20	401.0874	4.33	380.7192	4.11	393.4947	4.25	379.5392	4.10	406.8446	4.39	413.6865	4.46	387.6400	4.18	393.4347	4.25	393.1733	4.24	411.6103	4.44	411.2642	4.44	412.1764	4.45	378.5044	4.08	376.2809	4.06	413.6092	
8	381.8172	4.12	380.1215	4.10	380.4090	4.10	401.0179	4.33	389.4019	4.20	404.2396	4.36	389.8691	4.21	377.7635	4.08	400.2513	4.32	400.5190	4.32	412.6034	4.45	394.3428	4.26	411.0793	4.44	379.9773	4.10	375.2088	4.05	384.0392	
9	381.8783	4.12	386.4587	4.17	388.0531	4.19	377.6993	4.07	375.4333	4.05	382.0291	4.12	403.8283	4.36	399.9764	4.32	411.3956	4.44	396.2884	4.28	402.5865	4.34	396.3836	4.28	379.0636	4.09	406.8631	4.39	413.7041	4.46	392.4800	
10	402.5077	4.34	377.1291	4.07	400.9119	4.33	380.4045	4.10	398.8158	4.30	388.3430	4.19	413.3185	4.46	391.9084	4.23	400.8805	4.33	390.7145	4.22	388.4737	4.19	409.6719	4.42	385.3866	4.16	381.3629	4.11	403.5717	4.35	398.1698	
11	403.0617	4.35	393.9089	4.25	378.2956	4.08	411.3907	4.44	393.9272	4.25	393.9693	4.25	405.3116	4.37	405.5696	4.38	412.9882	4.46	375.5266	4.05	407.6583	4.40	400.5072	4.32	378.0969	4.08	397.1646	4.29	404.2730	4.36	409.5096	
12	379.8465	4.10	393.4044	4.24	408.0557	4.40	396.2526	4.28	395.0565	4.26	390.4568	4.21	393.4077	4.24	413.2471	4.46	408.4628	4.41	386.0701	4.17	413.5421	4.46	396.3285	4.28	390.8667	4.22	394.7958	4.26	410.3636	4.43	405.9688	
13	379.2332	4.09	398.8981	4.30	377.6276	4.07	395.8217	4.27	409.5206	4.42	377.3302	4.07	396.4267	4.28	401.0231	4.33	396.4440	4.28	388.0947	4.19	375.5357	4.05	400.1273	4.32	385.8838	4.16	404.6768	4.37	412.5023	4.45	411.7660	
14	378.3471	4.08	396.8436	4.28	396.7287	4.28	388.6179	4.19	401.7658	4.34	407.2105	4.39	406.1131	4.38	402.5833	4.34	380.6247	4.11	387.1798	4.18	399.5708	4.31	407.8518	4.40	400.2232	4.32	383.4101	4.14	390.1253	4.21	396.0795	
15	381.5336	4.12	376.2043	4.06	375.5022	4.05	390.3712	4.21	391.5394	4.22	397.2511	4.29	394.4026	4.26	390.9432	4.22	392.7156	4.24	386.3928	4.17	413.1298	4.46	414.6219	4.47	401.1543	4.33	398.8698	4.30	414.0020	4.47	395.8877	
16	398.4243	4.30	390.9921	4.22	383.0666	4.13	410.7709	4.43	409.3016	4.42	413.1675	4.46	400.5641	4.32	394.0594	4.25	399.9366	4.32	414.9000	4.48	387.0215	4.18	397.8269	4.29	380.6801	4.11	393.3717	4.24	393.8830	4.25	387.9976	
17	379.0219	4.09	383.7551	4.14	387.0855	4.18	412.9001	4.46	400.0286	4.32	405.4590	4.37	376.2733	4.06	383.2044	4.13	412.5682	4.45	410.9511	4.43	383.4167	4.14	389.2140	4.20	381.9887	4.12	407.6054	4.40	411.5560	4.44	406.8597	
18	405.3383	4.37	412.8171	4.45	378.3678	4.08	403.4806	4.35	400.6414	4.32	382.7257	4.13	400.6831	4.32	411.8770	4.44	400.4800	4.32	387.2997	4.18	397.8723	4.29	403.3712	4.35	385.7703	4.16	384.9859	4.15	384.9518	4.15	407.8064	
19	412.1208	4.45	396.3816	4.28	406.6192	4.39	400.9285	4.32	394.8774	4.26	398.9672	4.30	383.4447	4.14	375.3733	4.05	390.8871	4.22	406.0516	4.38	377.0367	4.07	377.6208	4.07	399.6402	4.31	408.0584	4.40	395.0738	4.26	400.1264	
20	402.1613	4.34	406.9674	4.39	380.5361	4.11	400.1251	4.32	399.3092	4.31	389.2953	4.20	411.4979	4.44	412.6112	4.45	382.9018	4.13	400.6207	4.32	403.8351	4.36	391.4121	4.22	394.7866	4.26	398.8597	4.30	388.9058	4.20	381.9213	
Temperature (Celcius)	26.0		26.0		26.1		26.1		26.1		26.2		26.2		26.3		26.3		26.3		26.4		26.4		26.5		26.5		26.5		26.6	
Relative Humidity (%)	59.2		59.1		59.0		58.9		58.9		58.8		58.7		58.6		58.5		58.4		58.4		58.3		58.2		58.1		58.0		58.0	

Image of Data Quality Audit

Quality Aspect	Analysis	Conclusion
Completeness	When scrolling horizontally to inspect the entire dataset, there are no missing values in any cell.	Acceptable
Consistency	The format of the data provided is unorganized and not ready for usage. The headers seem accurate as the values under the column/row represent what the header means. All headers and values are correct with no inconsistency in spelling or unit of measurement. The values are rounded off consistently, according to their respective column.	Acceptable
Validity	There are no outliers in any Weight and Height columns or Temperature and Relative Humidity rows. All values are logical and realistically possible. Not possible for duplicate observations as all values are varied in each sequence column, and they represent different timeframes. The metadata at the top of the sheet provides appropriate context to the dataset.	Acceptable

This concludes that the data is acceptable and can be further used for analysis as no data issues were found.

Data Preparation & Transformation

Steps	Reference Picture
Unpivot (melt) data of tablet observations to enable the dataset to be usable for analysis by Tableau. Justification for unpivoting in *Appendix 1.1* The dataset on this sheet contains the tablet and their information such as height and weight for all the timeframes. This sheet is the main dataset that will be used for analysis.	
Next, calculate the average mass of a tablet for each sequence. This value is needed for the Uniformity of Weight Test. To calculate the average mass, an excel formula was created and the 20 tablets were manually dragged for each timeframe to calculate the average mass at their respective times. Lastly the value was dragged for all the tablets in that same timeframe.	
Thirdly, calculate the percentage deviation of the tablet from the average mass during that sequence for the batch using the formula: $$\frac{\lvert average - mass \rvert}{average} \times 100\%$$ Percentage Deviation is required when deciding if a time sequence fails or passes the Uniformity of Weight Test.	
The acceptance criteria from the British Pharmacopeia Uniformity of Weight test were applied to determine if the tablet pass or fail the uniformity test. According to *Appendix XII C. BP's Table 2.9.5-1*, since the average mass for all sequences are above 250mg, the threshold for deviation will be no more than 5%. Any tablet that has a Percentage Deviation beyond 5% will fail.	

Next, the Temperature and Relative Humidity were transformed and melted into a columnar format to be used for analysis.

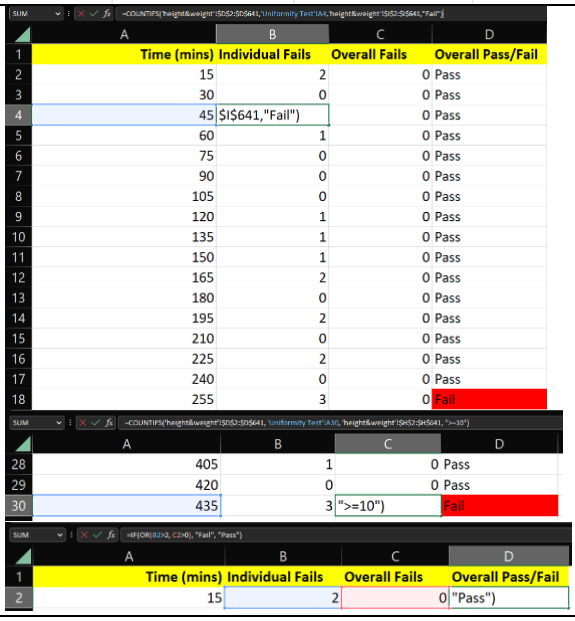
This dataset can be linked with the main dataset using Time (mins) as the common key.

Time (mins)	Temperature (Celcius)	Relative Humidity (%)
15	26	59.2
30	26	59.1
45	26.1	59
60	26.1	58.9
75	26.1	58.9
90	26.2	58.8
105	26.2	58.7
120	26.3	58.6
135	26.3	58.5
150	26.3	58.4

An Excel function is applied to count how many "Fails" there are for each timeframe. Using this function provides 100% accuracy, free from human error which could happen by manually counting.

Subsequently, an Excel formula is used to count the number of times a tablet has doubled the Percentage Deviation (5% x 2 = 10%) threshold as Overall Fails. If a sequence in the batch has more than 2 individual fails or if there is at least 1 overall fail, that sequence will fail the Uniformity of Weight Test.

This dataset keeps track of the sequences' overview statistics, to highlight what needs to be taken note of and brought up during analysis.



	A	B	C	D
1	Time (mins)	Individual Fails	Overall Fails	Overall Pass/Fail
2	15	2	0	Pass
3	30	0	0	Pass
4	45	I641,"Fail")	0	Pass
5	60	1	0	Pass
6	75	0	0	Pass
7	90	0	0	Pass
8	105	0	0	Pass
9	120	1	0	Pass
10	135	1	0	Pass
11	150	1	0	Pass
12	165	2	0	Pass
13	180	0	0	Pass
14	195	2	0	Pass
15	210	0	0	Pass
16	225	2	0	Pass
17	240	0	0	Pass
18	255	3	0	Fail

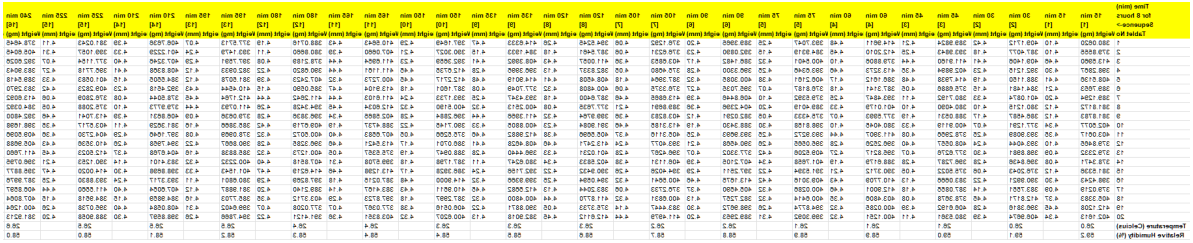
	A	B	C	D
28	405	1	0	Pass
29	420	0	0	Pass
30	435	3	">=10")	Fail

	A	B	C	D
1	Time (mins)	Individual Fails	Overall Fails	Overall Pass/Fail
2	15	2	0	"Pass")

A dataset to store metadata in a columnar format to be usable in Tableau was created

	A	B	C	D	E	F	G	H
1	Granulation:	Compressibility Index (%):	Hausner ratio:	Granules size range (µm):	Duration of tabletting (hour):	In-process control:	Name of product:	Company:
2	Dry granulation	25	1.34	600 to 1180	8	every 15 minutes	Maxeo tablets	Kanban Pharma Ltd.

Before:



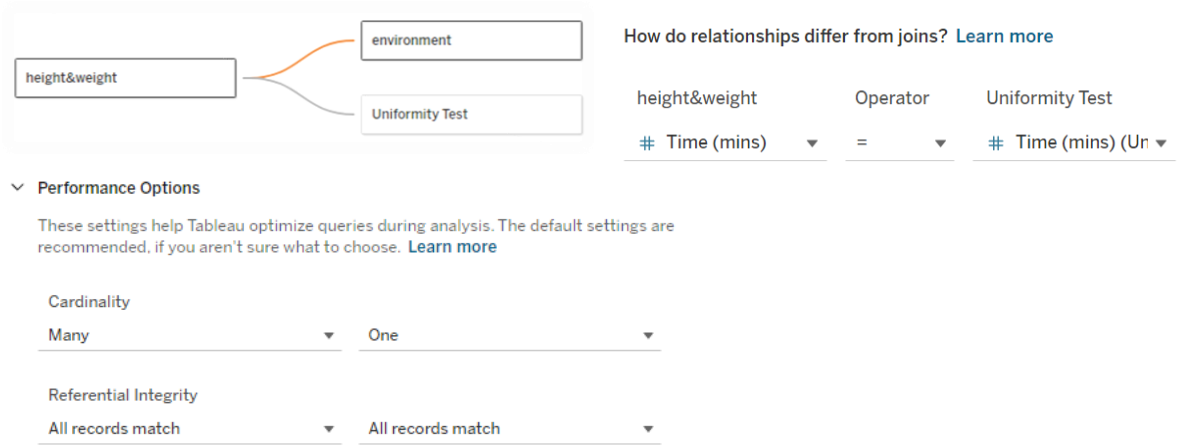
The data initially was in wide table format to facilitate readability.

After:

However, the format was changed into a tall table as this format is better for data analysis because it enables filtering, sorting, and aggregation, allowing for enhanced analysis.

Tablet No	Weight (mg)	Height (mm)	Time (mins)	Average mass at Time	Average - Mass	(Average-Mass)/Average	Percentage Deviation	Pass/Fail
1	380.0620	4.10	15	392.2250	12.1630	0.031010311	3.101031138	Pass
2	379.8555	4.10	15	392.2250	12.3695	0.031536795	3.153679487	Pass
3	413.5960	4.46	15	392.2250	-21.3710	-0.054486529	-5.448652919	Fail
4	398.2867	4.30	15	392.2250	-6.0617	-0.015454598	-1.545459798	Pass
5	408.5136	4.41	15	392.2250	-16.2886	-0.041528661	-4.152866128	Pass
6	389.7653	4.21	15	392.2250	2.4597	0.006271196	0.627119606	Pass
7	389.1294	4.20	15	392.2250	3.0956	0.007892459	0.789245928	Pass
8	381.8172	4.12	15	392.2250	10.4078	0.026535329	2.653532913	Pass
9	381.8783	4.12	15	392.2250	10.3467	0.026379551	2.637955121	Pass
10	402.5077	4.34	15	392.2250	-10.2827	-0.026216278	-2.621627758	Pass
11	403.0617	4.35	15	392.2250	-10.8367	-0.027628732	-2.76287321	Pass
12	379.8465	4.10	15	392.2250	12.3785	0.031559741	3.155974089	Pass
13	379.2332	4.09	15	392.2250	12.9918	0.033123384	3.312338412	Pass
14	378.3471	4.08	15	392.2250	13.8779	0.035382546	3.538254648	Pass
15	381.5336	4.12	15	392.2250	10.6914	0.027258383	2.725838347	Pass
16	398.4243	4.30	15	392.2250	-6.1993	-0.015805417	-1.5805417	Pass
17	379.0219	4.09	15	392.2250	13.2031	0.033662105	3.366210549	Pass
18	405.3383	4.37	15	392.2250	-13.1133	-0.033433053	-3.34330533	Pass
19	412.1208	4.45	15	392.2250	-19.8958	-0.050725423	-5.072542287	Fail
20	402.1613	4.34	15	392.2250	-9.9363	-0.025333111	-2.533311108	Pass
1	409.1712	4.42	30	393.2537	-15.9175	-0.040476494	-4.047649447	Pass
2	387.4077	4.18	30	393.2537	5.8460	0.014865646	1.486564639	Pass
3	409.1406	4.41	30	393.2537	-15.8869	-0.040398682	-4.03986821	Pass
4	392.1215	4.23	30	393.2537	1.1322	0.002878981	0.28789814	Pass
5	388.1150	4.19	30	393.2537	5.1387	0.013067062	1.306706178	Pass
6	384.1481	4.15	30	393.2537	9.1056	0.023154444	2.31544438	Pass
7	401.0874	4.33	30	393.2537	-7.8337	-0.019920297	-1.992029725	Pass
8	380.1215	4.10	30	393.2537	13.1322	0.033393636	3.339363622	Pass
9	386.4587	4.17	30	393.2537	6.7950	0.017278847	1.727884701	Pass
10	377.1291	4.07	30	393.2537	16.1246	0.041002974	4.100297398	Pass
11	393.9089	4.25	30	393.2537	-0.6552	-0.001666176	-0.166617644	Pass
12	393.4044	4.24	30	393.2537	-0.1507	-0.000383289	-0.038328949	Pass
13	398.8981	4.30	30	393.2537	-5.6444	-0.014353153	-1.435315276	Pass

Data Integration
The finalised dataset was loaded into Tableau.



Configurations to link datasets
Linked environment and Uniformity Test to height&weight dataset using Time as a Common Key.
Cardinality: Many-to-One because height&weight dataset has repeated Time values; A record in environment or Uniformity Test dataset is related to many rows in height&weight table.

Relationships
The datasets were connected using Relationships in Tableau as it is more flexible than Joins since Relationships are dynamic, hence preserving the granularity of the different datasets while allowing them to be integrated and used together. This allows for easier management of data as errors can be rectified easily without needing to manually update each row when there are changes or corrections made to the underlying data, making it more versatile to work with than traditional joins.

Data Storytelling

Insights from Exploratory Data Analysis

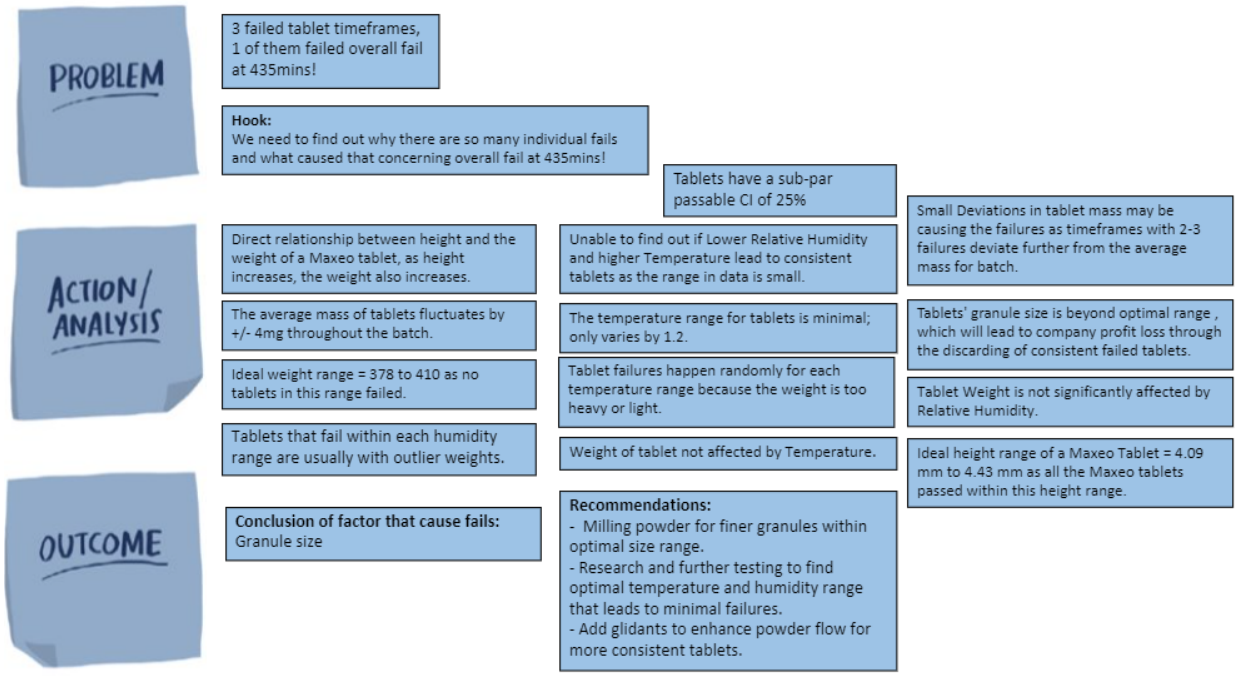
- 3 failed tablet timeframes, 1 of them failed overall fail at 435mins!
- The temperature range for tablets is minimal; only varies by 1.2.
- Weight of tablet not affected by Temperature.
- Tablet failures happen randomly for each temperature range because the weight is too heavy or light.
- Ideal weight range = 378 to 410 as no tablets in this range failed.
- Lower Relative Humidity and higher Temperature could lead to more consistent tablets that don't fail.
- The average mass of tablets fluctuates by +/- 4mg throughout the batch.
- Weight does not seem to be affected by Relative Humidity.
- There is a direct relationship between the height and the weight of a Maxeo tablet, as the height increases, the weight also increases.
- Small Deviations in tablet mass may be causing the failures as timeframes with 2-3 failures deviate further from the average mass for batch.
- Tablets that fail within each humidity range are usually outlier for their weights.
- Tablets have a sub-par passable Compressibility Index of 25%
- Ideal height range of a Maxeo Tablet would be from 4.09 mm to 4.43 mm since all the Maxeo tablets passed within this height range.
- Tablets' granule size is beyond optimal range , which will lead to company profit loss through the discarding of consistent failed tablets.

Big Idea : Maxeo Tablet batch quality check

Who's the Audience?	List primary group or individuals	Kanban Pharma Ltd
	If narrow down to one, who?	Head of Production for Maxeo Tablets
	What do they care about?	Whether the tablet batch passes British Pharmacopeia Uniformity of Weight standards, to know if the tablets are of acceptable quality.
What's at stake?	What are the benefits?	Improved Maxeo Tablet batch quality, adherence to Pharmacopeia standards, reduced expenses from regulatory penalties and operational costs from remaking tablet batches.
	What are the risks?	Non-compliance with pharmacopeia standards may result in product recalls, regulatory penalties and tarnish Company's Reputation.
	What's the urgency?	Urgent action needed to avoid manufacturing issues, ensure consistent Maxeo tablet quality, regulatory compliance, and customer safety.
	Action needed from audience	Promptly take actions to address the problems found in manufacturing process.
What's the Big Idea	In one sentence	Find out factors that cause Maxeo Tablets to fail Pharmacopeia standards so that they can be promptly addressed by stakeholders, to avoid loss of money from remaking batches so that Kanban Pharma Ltd doesn't face regulatory penalties and product recalls which could also tarnish their reputation.

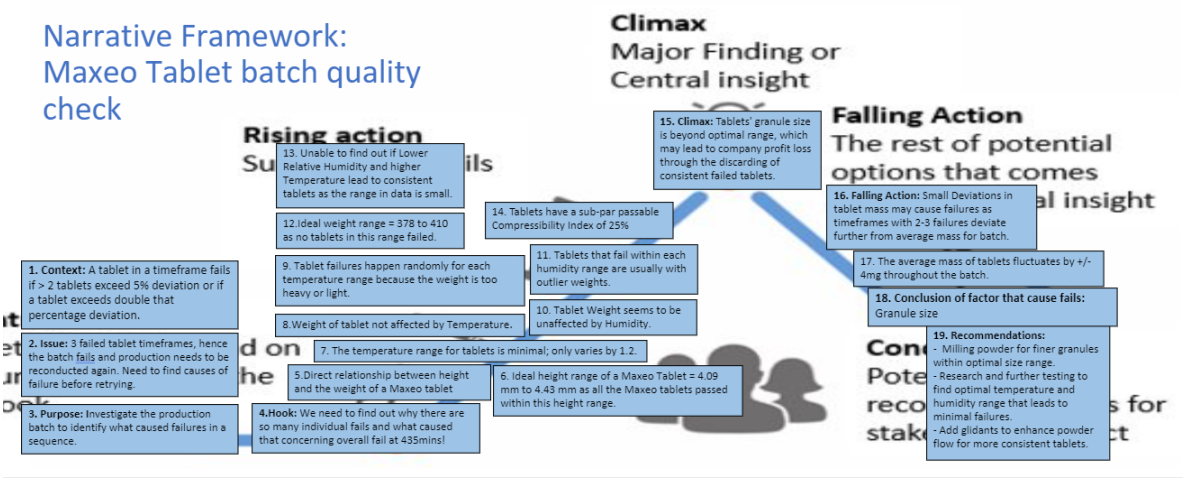
Action: The Head of Production needs to know issues with tablet production, so that it can be fixed before producing the next batch of Maxeo tablets.

Linear Storyboard



Narrative Framework

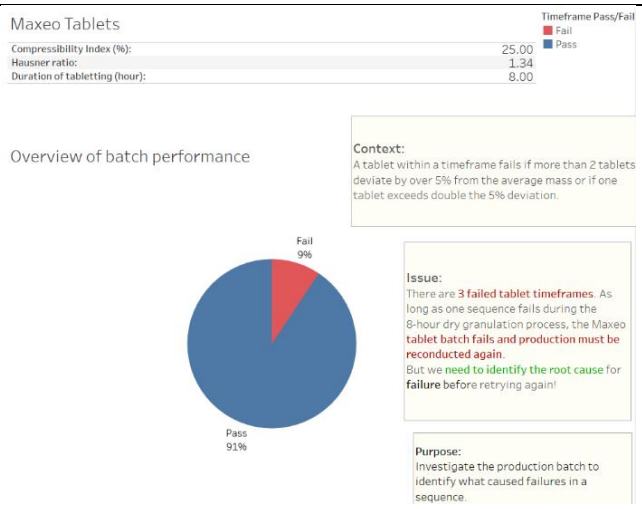
Freytag's Pyramid Narrative Framework is applied to create a storyboard to express the insights to the stakeholders in a linear fashion that resembles a story flow to be engaging and make the insights memorable.

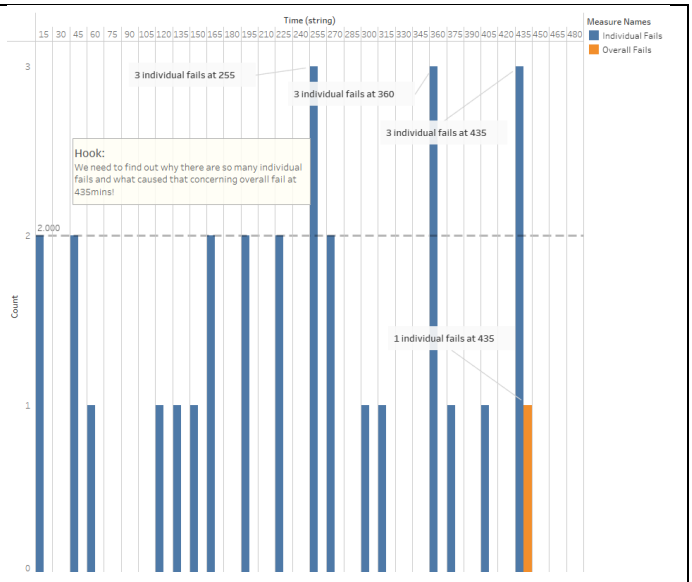
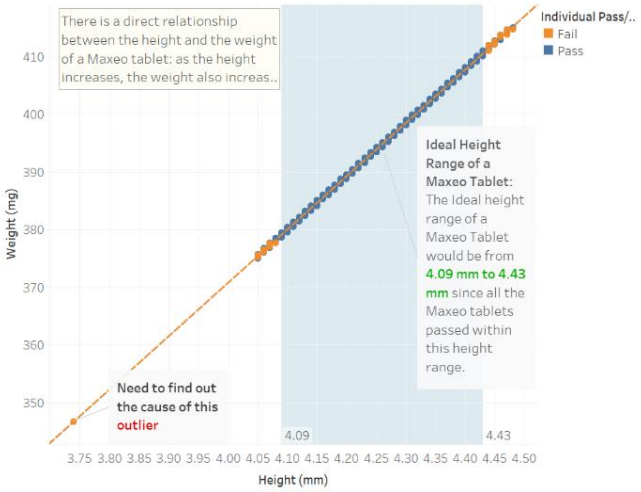


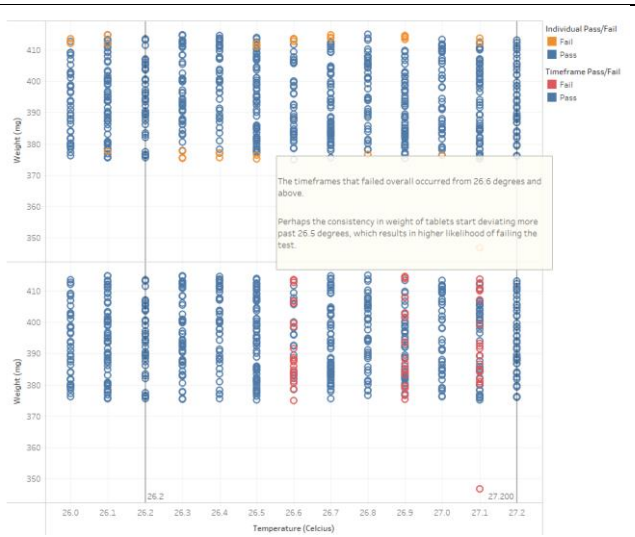
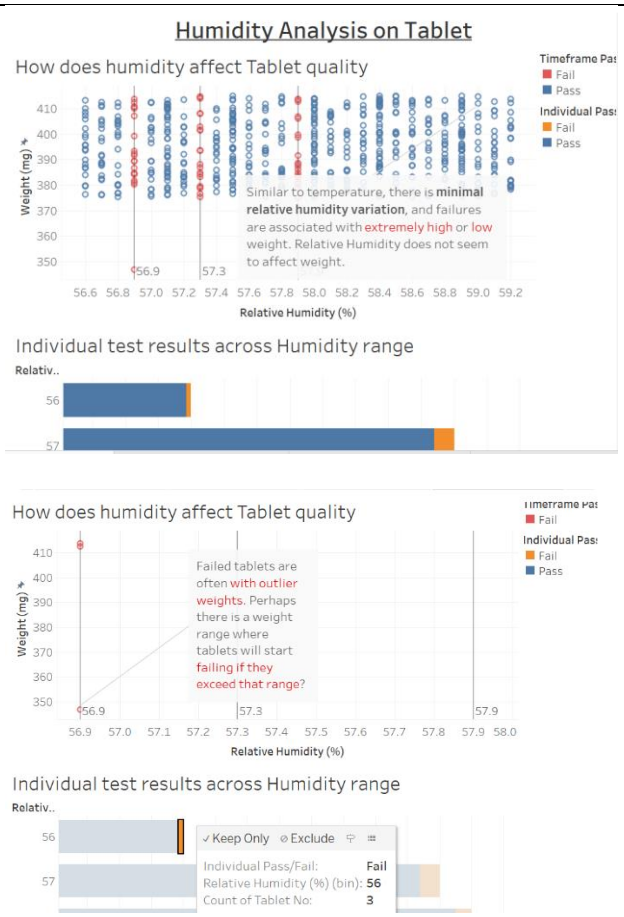
Overview of How the Insights were Structured according to the Narrative Framework

The main highlight of this Framework is the Hook which is the introduction that gets the Head of Production interested in wanting to find out more about story. Following the Hook is the Rising Action which is the build-up to Climax which is the most interesting and crucial peak moment of story. Finally, the Falling Action build follows to the resolution, which is concludes the story.

<u>How the Freytag's Pyramid will be applied to the Data Storyboard</u>

Overview of batch performance (Introduction) To begin, what determines a pass or fail for British Pharmacopeia Uniformity of Weight Test was briefly explained as context to recap to the Head of Production and to showcases knowledge in this area. The issue found in the analysis was included to let the Head of Production know it is necessary to explore why because this batch failed the BP Uniformity of Weight Test, and the purpose is to let Production Head know what they can benefit from this investigation. The pie chart is used to show the proportion of timeframes that passed and failed to get an overview understanding of how well the batch performed for BP Test throughout the 8-hour duration.	

Failure statistics in visual form (Hook): A dual axis was used to effectively show number of individuals fails and overall fails for each timeframe. Colour-coding differentiates individual fails and overall fails intuitively using visual aid. The colour orange was chosen to differentiate the more severe overall failure from an individual fail which was blue in colour. Reference lines were added at y=2 to let Production Head visually compare with the threshold that leads to an overall fail. Annotations were added to inform the reader of the insights directly, as it is challenging to read the x-axis due to the multiple columns.	
How weight and height of tablet are related: There is a direct linear correlation between the weight and height of a tablet and by plotting a scatterplot how weight increases as height increases can be observed. A diagonal reference line was added to clearly show that the weight and height relationship is linear. Color-coded observations (dots) to uncover insight of the height and weight of all passed and failed tablets to visualize the trend. A reference band was added to highlight the ideal table height range which facilitates readers to capture the insight where no tablets failed and included the range of table height values which is easier to read. As for the legend the same colours were used to represent individual pass and fail to establish conventional understanding across all graphs in story.	

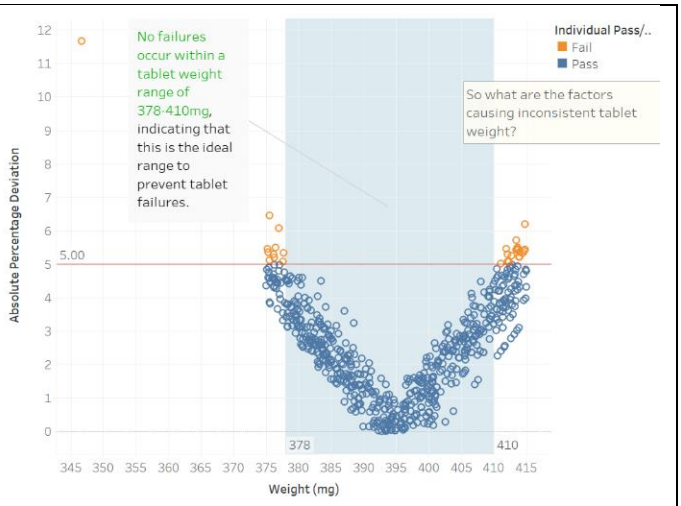
How temperature affects tablet weight: This chart compares how the tablet weight varies across different temperatures. To facilitate insights, there are 2 identical graphs. The top graph is coloured by individual pass or fail, while the bottom graph is coloured by Timeframe pass or fail , which is when 3 tablets failed. The tablet temperature variation is minimal of 1.2 degrees, and tablet weight shows no correlation with temperature.	
How humidity affects tablet weight: This dashboard allows the Head of Production to analyse how the tablet weight varies across different humidity. It allows the target audience (Production Head) to filter the observations in the scatterplot using the bars in the bar chart. The bar chart is composed of tablets that passed and tablets that failed, to let the readers compare the count of tablets within each humidity bin and visualize the composition of how many pass-fails there are in each humidity bin. If the Production Head wants to investigate deeper, they can click either the blue or orange bar of a timeframe to find out the weight of those tablets to compare their weight with other tablets which can be seen in the graph of how Humidity affects Tablet quality. The insight to take away from this dashboard is that tablets that failed are often outliers and this is shown by duplicating the dashboard in the next slide and fixing the configurations, so the Head of production does not have to click and investigate to find this insight out themselves. Failed tablets are with outlier weights, thus the minimum range threshold to when tablets will start to fail should be identified… building up to the next slide.	

How percentage deviation varies across weight:

This scatterplot shows a clear trend that tablets only start failing when the weight falls beyond the ideal range of 378 to 410mg.

This claim can be made because there is a clean cut between the range's thresholds, and no individual fails fall within the range.

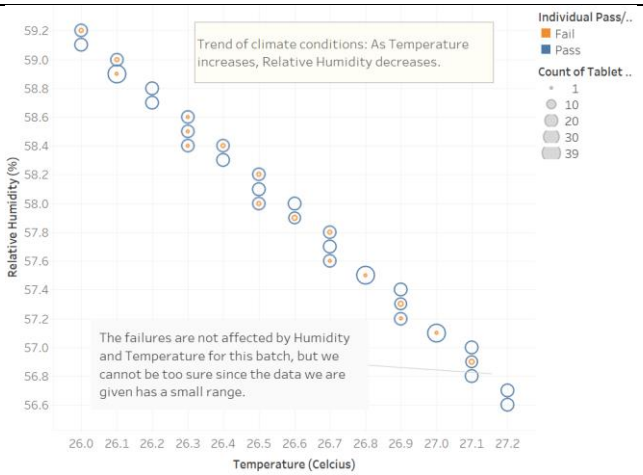
The pattern was found to determine what causes a tablet to fail. However, need to find out what causes a tablet's weight to deviate beyond this ideal range.



Interpreting how Humidity and Temperature affects weight:

This scatter plot shows a decreasing trend when Relative Humidity of tablet (RH) decreases and, Temperature of tablet increases.

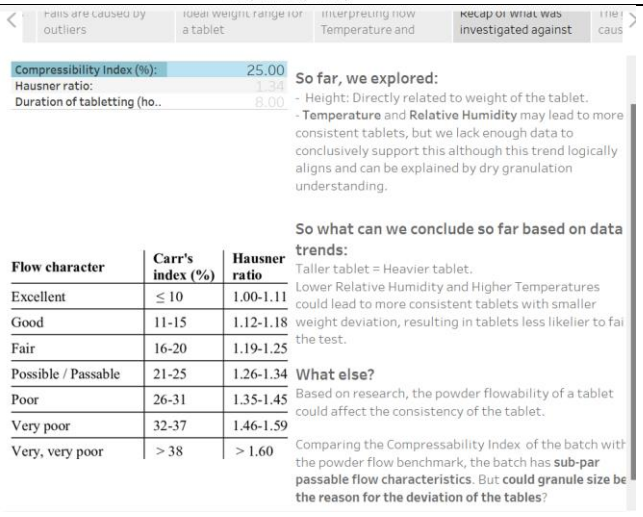
It further supports that there is no clear pattern between consistent tablet size and RH and Temperature. However, this cannot be confirmed as the data range is too small to jump to any conclusions.



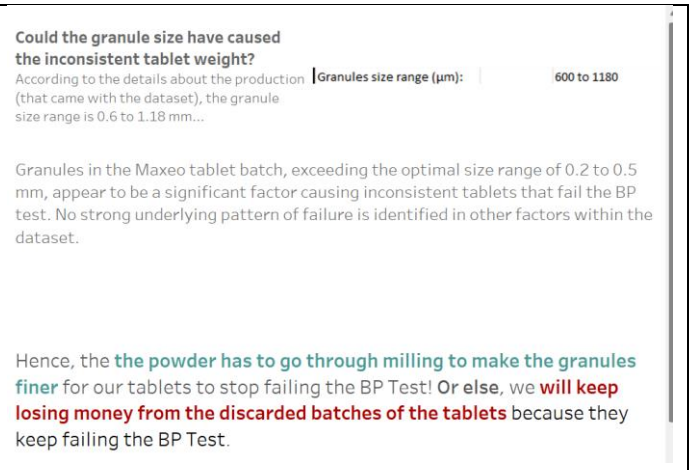
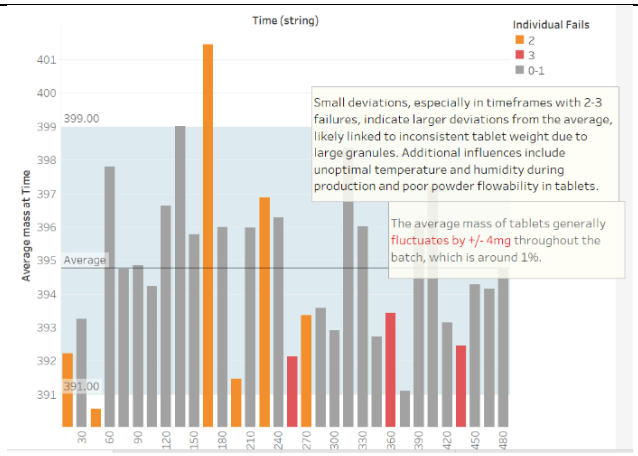
This recap page lets the Production Head recall what has been covered so far and where the analysis is heading before the climax where the true driver is revealed.

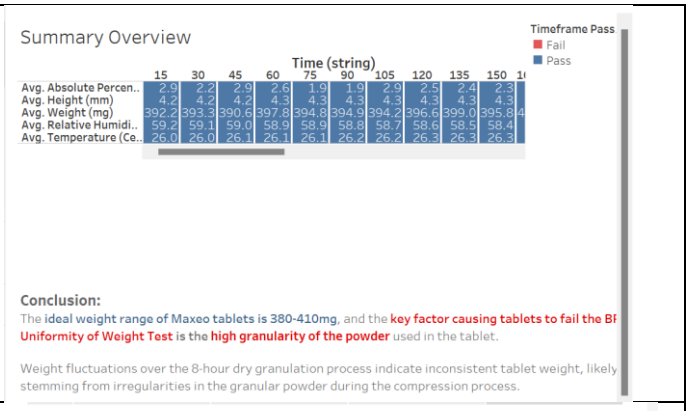
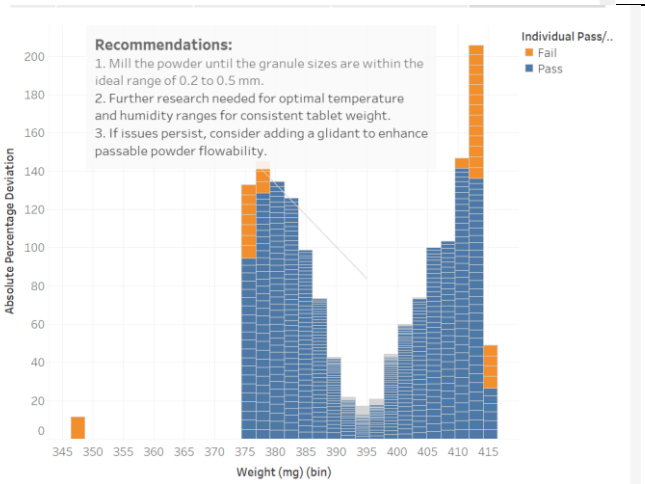
External research was included to further draw connections between how the Compressibility Index (CI), also known as Carr's Index, could be related to tablet weight. Then, the CI for this batch was compared to a table to identify and determine that the powder used in this tablet batch had a sub-par passable flowability.

This page builds up to the climax where the granule size is analyzed and found to be the main cause for inconsistent weight in tablets which resulted in the fails.



Flow character	Carr's index (%)	Hausner ratio
Excellent	≤ 10	1.00-1.11
Good	11-15	1.12-1.18
Fair	16-20	1.19-1.25
Possible / Passable	21-25	1.26-1.34
Poor	26-31	1.35-1.45
Very poor	32-37	1.46-1.59
Very, very poor	> 38	> 1.60

Possible main reason of inconsistent weight tablets and why it must be addressed (CLIMAX): This dataset shows that the granule size range is 0.6mm to 1.18mm, which falls outside the optimal granule size range of 0.2mm to 0.5mm for Maxeo tablets during granulation. Therefore, the large granule size(outside of optimal range) could be the most significant factor causing the inconsistent weight for Maxeo tablets in our batch. To prevent repeated failures of the BP Uniformity of weight test, the powder should go through milling to achieve finer granules. This is crucial to help Kanban Pte Ltd avoid losing money due to the discarded batches of failed Maxeo tablets.	
How tablet mass fluctuates across timeframes (falling action): This bar chart shows how the average mass for each timeframe varies from the average mass for the batch to assess the fluctuation of the tablet mass overall. To compare the variation with average, besides adding a trend line, a reference band was used to colour a range of +/- 4mg from the average. To facilitate the insight of showing how these fluctuations may potentially influence the tablets, the bars were color-coded based on how many individual fails there are. The 0-1 fails were grouped as grey to avoid using many colours to make the graph overly bright. This graph helps support the recommendations of how the failures could be linked to the flowability of powder by showing the average masses are inconsistent which could be caused by poor flow.	

Resolution: The analysis was concluded by providing a conclusion and recommendations. A table chart was included for readers (Production Head) to explore and get an overview of tablets for each timeframe.	
Call to action: The recommendations are sequenced from most important at the top, to least important as the last. This slide is needed to remind the reader to take action to resolve the issues found from the analysis. The chart is added to convince the Production Head to act on the proposed recommendations so that the issues which is shown in the chart (tablets failing) in production can be resolved. A stacked bar chart was created of absolute percentage deviation against weight (bin) to clearly show that tablets never failed individually if the weight is between the proposed weight range, proving to the Production Head that the recommendation proposed is supported by a clean pattern so they will be more convinced to take action.	

Conclusion and Recommendations

According to the data obtained from the visualizations, three different factors play a part in affecting the uniformity of weight of the tablets. Powder flowability, relative humidity, and granule size, with granule size being the main factor that affects the uniformity of weight of the Maxeo tablets.

Granules in the pharmaceutical industry are mainly generated as an intermediary with a size range of 200 µm to 500 µm. The granule size according to the dataset, they are in the range of 600 µm to 1180 µm which exceeds the ideal granule size range. Large granule size in tablet manufacturing can lead to several issues. Firstly, it may cause blend inhomogeneity, where differences in densities and compositions between large and small granules result in weight discrepancies among individual pills. Secondly, segregation during tablet compression and storage can occur, causing uneven distribution of drug content and resulting in tablets with varying weights. Additionally, large granules often exhibit poor flow qualities compared to smaller particles, leading to uneven tablet die filling and inconsistent tablet weights. Moreover, variations in compression forces may be needed for larger

granules, further contributing to weight discrepancies in the final tablets. Therefore, larger granule size such as the one in the dataset is not recommended for tablet manufacturing.

To reduce the large granule size of 600µm to 1180µm milling can be conducted. Milling is the process of reducing bigger particles into smaller ones. Granules get reduced in size during milling, which makes the granule size finer and more consistent. This enhances the granule flow characteristics and helps achieve greater uniformed content in the tablet formulation.

The powder flow of the Maxeo tablets led to the inconsistency in the weight of the tablets. Hausner ratio and Compressibility Index is used to indicate the tendency of the powder to be compressed and settled which shows the significance of interparticle interactions between the powder. The Haunser ratio stated for the batch of Maxeo tablets is 1.34% and the Compressibility Index is 25%. According to *Appendix 1.1,* the Maxeo tablets powder flow is passable. When the powder flow is passable, it shows the presence of larger interparticle interactions, meaning that there is a greater difference between the bulk and tapped density of the Maxeo tablet powder.

The idea behind these techniques is that cohesive powder, which forms many bridges when particles are loosely packed, does so because of cohesive connections that are formed at the points of contact between the particles. These cohesive bonds are destroyed when the powder bed is tapped. Because less cohesive powders do not develop the bridging cohesive bonds, the powder bed collapses to a smaller volume and a greater density. In contrast, less cohesive powders do not undergo as much change in bulk density. As a result, smaller bulk density and tapped density variations brought on by tapping are suggestive of a well-flowing powder because they avoid the formation of cohesive bonds or significant bulk density changes. Thus, the Maxeo tablet powder flow is passable, it does not suggest a well-flowing powder hence, leading to the inconsistent uniformity of weight.

Adding a glidant improves powder flowability through several mechanisms. Firstly, it reduces interparticle friction by acting as a lubricant and creating a slippery layer on the particle surfaces. This promotes easier sliding between particles. Secondly, glidants enhance particle size distribution, ensuring a more uniform distribution and smoother flow. Thirdly, they optimize powder density by reducing void spaces, increasing bulk density, and minimizing resistance during particle movement. Lastly, glidants prevent caking and clumping by creating a barrier between particles, hindering their tendency to stick together. Examples of suitable glidants for experimentation include corn starch or talc at a 5% concentration.

When the relative humidity of the tablet was at 56.9%, 57.3% and 57.9%, the tablets failed the Uniformity of Weight Test. This indicates that the relative humidity affects the consistency in weight of tablets and when the production is done, the relative humidity should be kept from ranges 56.6% to 56.8% or 57% to 57.2% or 57.4% to 57.8% or 58.0% and above to ensure that the tablets are uniform so that the quality is higher. At the ranges of 56.6% to 56.8%, 60 tablets passed which is 9.38% of the overall tablets. From range 57.0% to 57.2%, 60 tablets also passed which is a 9.38% of the overall tablets. From the range 57.4% to 57.8%, 100 tablets passed the Uniformity of Weight Test which is 15.6% of tablets pass. However, most tablets that passed is within the range of 58.0% and 59.2% and it is 43.8% of the total tablets. The weight of the tablets tends to be more consistent at lower humidity ranges. Unfortunately, according to the dataset the humidity ranges from 56.6% to 59.2% which is very minute, therefore there is insufficient evidence to prove the claim made.

Wet granulation is a common method of producing tablets in the pharmaceutical manufacturing industry. To get the small particles in a mixture to clump together into granules with the right size

and flow characteristics, water or an organic solvent can be poured or sprayed on it. While wet granulation is a method that can also use for the production of Maxeo tablets, Dry granulation is sufficient if the recommendations made are put into place to ensure better flowability and uniformity of tablets.

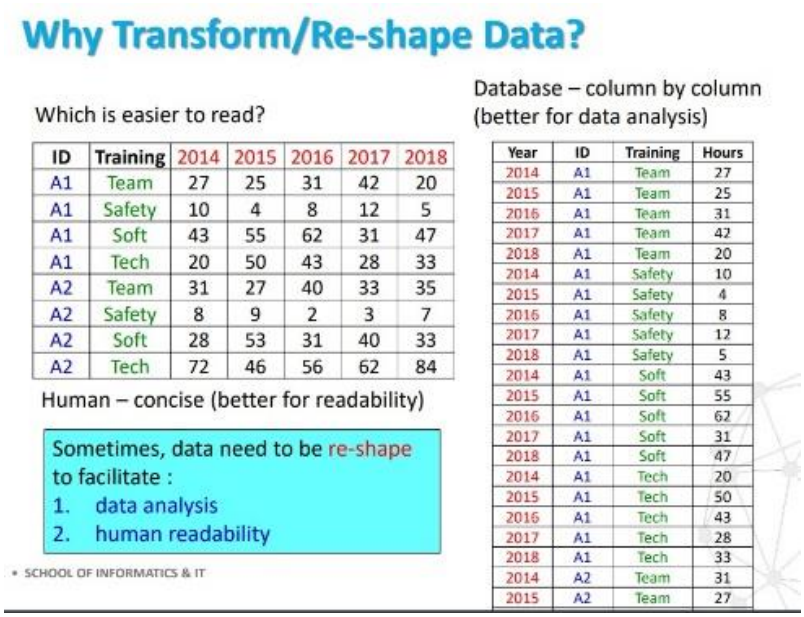
To summarise, the Maxeo tablets had inconsistent weight which is seen in the failure of the Uniformity of Weight test. The major factor that caused the Maxeo tablets to fail is the granule size of the powder, which can be refined by the process of milling. Another factor that could affect the results is the powder flowability which can be improved with the addition of glidants. Thus, the manufacturing process of Maxeo tablets must be halted until the recommendations are put in place during production to ensure that the Maxeo tablets are of high quality before they can be released into the market for patient use.

Ensuring the recommendations are put into place will ensure no profit loss as the tablets would pass the Uniformity of weight tests and not have to be discarded, benefitting kanban Pte Ltd as a company from not wasting resources.

Appendix

Compressibility Index (%)	Flow Character	Hausner Ratio
≤10	Excellent	1.00–1.11
11–15	Good	1.12–1.18
16–20	Fair	1.19–1.25
21–25	Passable	1.26–1.34
26–31	Poor	1.35–1.45
32–37	Very poor	1.46–1.59
>38	Very, very poor	>1.60

Appendix 1.1 ,USP42-NF37: ⟨1174⟩ POWDER FLOW



ID	Training	2014	2015	2016	2017	2018
A1	Team	27	25	31	42	20
A1	Safety	10	4	8	12	5
A1	Soft	43	55	62	31	47
A1	Tech	20	50	43	28	33
A2	Team	31	27	40	33	35
A2	Safety	8	9	2	3	7
A2	Soft	28	53	31	40	33
A2	Tech	72	46	56	62	84

Year	ID	Training	Hours
2014	A1	Team	27
2015	A1	Team	25
2016	A1	Team	31
2017	A1	Team	42
2018	A1	Team	20
2014	A1	Safety	10
2015	A1	Safety	4
2016	A1	Safety	8
2017	A1	Safety	12
2018	A1	Safety	5
2014	A1	Soft	43
2015	A1	Soft	55
2016	A1	Soft	62
2017	A1	Soft	31
2018	A1	Soft	47
2014	A1	Tech	20
2015	A1	Tech	50
2016	A1	Tech	43
2017	A1	Tech	28
2018	A1	Tech	33
2014	A2	Team	31
2015	A2	Team	27

Appendix 1.2, Justification for unpivoting, screenshot from Brightspace lecture notes

References

Alei. (2022, August 10). Wet granulation VS Dry granulation. AIPAK. https://www.icapsulepack.com/the-wet-granulation-vs-the-dry-granulation/#:~:text=Wet%20granulation%20is%20considered%20best,while%20dry%20granulation%20makes%20tablets

Bulk density - US pharmacopeia (USP). USP.ORG . (n.d.). https://www.usp.org/sites/default/files/usp/document/harmonization/gen-chapter/20230428HSm99375.pdf

Hausner ratio. Hausner Ratio - an overview | ScienceDirect Topics. (n.d.). https://www.sciencedirect.com/topics/nursing-and-health-professions/hausner-ratio

How Relationships Differ from Joins. (n.d.). Tableau. https://help.tableau.com/current/online/en-us/datasource_relationships_learnmorepage.htm

Jakubowska, E. (2021, November 11). Blend Segregation in Tablets Manufacturing and Its Effect on Drug Content Uniformity—A Review. National Library of Medicine. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8620778/

Kotamarthy, L., Metta, N., & Ramachandran, R. (2020). Understanding the effect of granulation and milling process parameters on the quality attributes of milled granules. Processes, 8(6), 683. https://doi.org/10.3390/pr8060683

Li, J., & Wu, Y. (2014, February 25). Lubricants in pharmaceutical solid dosage forms. MDPI. https://www.mdpi.com/2075-4442/2/1/21#:~:text=To%20improve%20the%20flowability%20of,the%20inter%2Dparticle%20adhesion%20force

Pharmaguideline. (n.d.-a). Effect of humidity level on tablet stability. https://www.pharmaguideline.com/2018/09/effect-of-humidity-level-on-tablet-stability.html#:~:text=All%20samples%20used%20showed%20deterioration,which%20adversely%20affects%20its%20hardness

Shanmugam, S. (2015). Granulation techniques and technologies: Recent progresses. BioImpacts : BI. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4401168/

Swiss, A. (n.d.). What is granulation? | Acino.

https://acino.swiss/our-business/contract-manufacturing/case-studies/what-is-granulation#:~:text=Wet%20granulation%20is%20a%20widely,size%20with%20required%20flow%20properties