CMC Workshop At September 2009 OutSourcing Conference

Problem Statement

A biotech has just in-licensed a Phase 2a clinical oncology candidate that has been given fast track status on September 15, 2009 and the company received $100 million in funding to move the candidate through development to commercial.

Your group has been given a budget of $5 million as a part of the total funding to manage the process development and manufacturing. The funding you have will need to be sufficient for you to supply API and Drug for the Phase 2b program, Phase 3 and the work required to scale-up and establish commercial supply. You will need to line up the supply chain for Phase 2b, all Phase 3 clinical trial materials, backup supply of API, intermediates suppliers and formulation/final dose manufacturing. According to the dosing schedule established in Phase 2a, patients are given 16.8 gm API for one cycle (28 days, 3 months). The dosing for Phase 3 is expected to be the same but will be two cycles (6 months), double the Phase 2b treatment.

You have been told the cost of the current manufacturing of API is $65,000 per kg (not including the final dosage manufacturing, packaging) and the projected commercial launch volume is 500 kg for a market of approximately 3,600 kg/yr. The licensor has also provided two quotes for Phase II API supply from potential commercial suppliers, one for k$45/kg and one for k$40/kg (CMO A and CMO B, respectively). The current API supplier can handle Phase 2 supply and "probably" Phase 3 supply but cannot handle the commercial volumes in their cytotoxic facility.

You will need to start production of the API for the Phase 2b trial (90 patients) as soon as practical since it is the rate-limiting step for the start of your company's clinical trial program. To keep the program on track and avoid delays, you will need to initiate production of Phase III API (750 patients) by 3Q 2010.

This API is dosed as a 100 mg tablet manufactured by wet granulation. The tablet manufacturer has no volume limitations but will need to scale up for commercial production. However, the technical package reveals there are multiple polymorph forms -- all of which have appeared in different API batches manufactured by the current supplier. Production of tablets, including primary and secondary packaging, is about $0.75/tablet on a placebo basis.

You have been asked to give an overall development plan from start to finish within the next month to accomplish the timelines and challenges facing this program.

Discovery Information for Workshop Participants

1. **If prompted about API process and cycle time.**

   a) API process has 8 synthetic steps. Depending on the amount of equipment available to dedicate, the CMOs can run one batch in about 2-4 weeks/batch.

   b) Give information from CMO summary on batch size and cycle.

2. **If prompted about material availability from licensee**

   a) The old CMO has samples of three API batches in retains, 5, 20, and 100 grams, which turn out to be polymorphs (PM) I, II, and III, respectively. You also have 500 gm of unused API of PM III which could be used for formulation studies.

3. **After a group develops a plan to evaluate the API polymorphism and select the most stable polymorph, the following can be revealed:**

   a) Your study of the chemistry of the polymorphism takes 2 months to complete and costs k$150. You learn the following:

   b) Thermodynamic evaluation shows PM I is stable at room temperature and PM II/III are stable at temps > 45 °C. Your stability data shows only 1 year stability for the PM II/III batches. You have no stability for the PM I batch.

   c) PM I is converted to PM II/III at temperatures > 50 °C if enough water is present. PM II/III can be converted to PM 1 by re-crystallization at <40 °C and a slightly different solvent concentration. Your API process is readily adjusted

4. **If prompted about polymorphism impact on the drug product formulation**

   a) Analysis of the tablet retains shows all polymorphs in the lots made from PM II/III and some PM II in the batch made from PM I API. There appears to be no difference in tablet stability but dissolution barely meets specs when there is a high percentage of PM II or III.

   b) A study of the granulation and drying conditions of drug manufacture shows PM I can be converted under conditions of excess moisture/temperature. Adjustment of the formulation process yields only PM I if only PM I API is used.

5. **If prompted by questions about various conditions at the candidate CMOs, the information on the attached page can be given, by category, using the "clue slips"**

INFORMATION WHICH MAY BE DISCLOSED TO WORKSHOP PARTICIPANTS IN RESPONSE TO QUESTIONS

CMO & Quote	Max Batch Size/Cycle	Location/ Availability	Compliance	Operations, Business and Other Information
Old CMO k$65/kg	2 kg 4 weeks	US/EU 1 month	1. 2002 EMEA Audit OK 2. Weak on OOS investigations. 3. Your audit turns up 2 major, 5 minor items.	1. Original manufacturer of API. 2. Willing to work with you on solving the polymorph problem. They have experience in this issue.
CMO A k$45/kg	40 kg 2 weeks	US/EU 4 months	1. OK FDA/EMEA Audits in 2006, none since. 2. VP of QA left after 2006 audits. 3. Your audit turns up no major items and a few minor items	1. Is currently performing chemistry similar to your API. 2. Willing to discount price to k$38/kg upon commitment of launch vol. API. They have indicated you will need to help pay for capital of the expansion if they commit to the lower price. 3. Expansion of the cytotoxic production suite is planned, will raise batch capacity to 60 kg/batch. 4. Need to have commitment to order within the next two weeks. Otherwise facilities will be used for another project which will run until May 2010.
CMO B k$40/kg	50 kg 2 weeks	Emerging Market 3 - 6 months	1. No audits. 2. Your audit turns up 2 major items and a systematic weakness in the Quality system. 3. They express great eagerness to learn from your expertise because they have very inexperienced QA people.	1. Basic in the Starting Materials (SM) for your API. 2. Will need to explore API chemistry in lab to commit. 3. Will go to k$35/kg "or lower" if you commit to purchase SM from them. 4. They make APIs for domestic use but none for export. 5. Their parent company, which produces Drug Products for domestic use was implicated in government bribery scandal, but nothing was proved. One of the manufacturing plants of the parent company received a warning letter, which is in the process of being resolved.
CMO C k$30/kg	70 kg 2 weeks	Emerging ex Soviet Bloc 6 months	1. No CMC audits, but some major Pharma companies are using their clinical trial subsidiary. 2. Delay scheduling the audit. Facilitator cannot give immediate answer. 3. Audit turns up 3 major items but a very large number of minor items. 4. They do not currently handle Cytotoxics and are not currently producing APIs	1. *Their patent just issued on a novel route to make your API. The polymorph forms of the API are disclosed in the patent.* 2. The process to make the polymorph is not part of the claims and there is no composition of matter patent on the polymorphs since they were disclosed at a public scientific meeting 2 years previous to the patent filing date. You do not infringe. 3. Their route uses a different Starting Material from your current chemistry. 4. No negotiation on price because of their proprietary position. 5. They are currently practicing this similar chemistry on the 70 kg scale for a custom intermediate. 6. No good control on protection against cross contamination

Guide to Solution of API Sourcing Problem

Please note that this document is strategic in nature and was developed for educational purposes. It does not constitute regulatory advice for any specific condition or program.

This document provides a possible solution to the API sourcing problem. Many aspects of the program can be run differently and still satisfy the program needs. The major points which need to be considered and elements pertinent to the decision making are outlined below.

Phase 2b Trial Supply

1. **The polymorph (PM)** issue must be resolved before Phase 2b since polymorph state may affect critical to quality (CTQ) attributes of API identity and stability, the drug manufacturing process, and drug dissolution and degradation, including shelf life.

    a) Identify a contractor and perform thermodynamic evaluation on API and drug samples to characterize nature of PMs. You have no fresh API available, so you will need to make some in the lab to evaluate what happens upon aging.

    b) Develop and validate method to identify polymorphs (PM) in the API and Drug Product.

    c) Evaluate API chemistry at contract lab or old CMO for ways to control formation of PMs and/or interconvert forms. Use left over 500 gm API to create 250 gm of PM I. Define conditions that control formation of PM I and how to convert some of the old API to PM I.

    d) Use old samples of API, including the API converted to PM I to evaluate impact of drug manufacturing process on control/interconversion of polymorphs.

    e) Evaluate batches of Drug for PM content and correlate with quality parameters such as dissolution and degradation upon storage.

    f) Use batches of API produced for Phase 2b to "demonstrate" control (QbD element) of correct polymorph formation. Do the same for the Drug Product and control of granulation/drying.

    g) Carefully evaluate stability and other quality properties of API & Drug in storage stability studies.

    h) Perform equivalency studies to link pharmaceutical and toxicological properties of PM I API with previous studies.

2. **API Supply**: You should include overages for issues related to supply chain, patient washouts and changes in patient numbers, as well as compassionate use. Quantities to target for delivery could be the following:

    a) Clinical Trial (CT) requirements for Phase 2b -- 90 patients (PTs) @ 168 tablets or 16.8 gm/PT. This quantity has NO contingency.

i. Add an overage of at least 15% to account for dead inventory in the CT system, partially used bottles, and operating losses. This translates to 20/gm PT or 1.80 kg for 90 PT.

ii. Add 15% (typical at pilot scale) for losses of API during the formulation process and 20% contingency for additional PTs = 2.65 kg.

b) Make an extra 3-4 kg for formulation development studies and make at least three batches. This can be the opportunity to perform the effect of variable studies needed to define the basis for the commercial API process and demonstrate stability.

i. Since the batch size at old CMO is 2 kg, make 3 batches to demonstrate new PM process and product quality, and gather data for scale-up = 6 kg.

c) In general, at this stage in development -- until the process has been validated on scale, the API manager should be cautious against yield "erosion" compared to lab or even previous scale results. Until the effects of variables (EOV) are well-understood, obtaining a yield of 5-10% below target is not unusual, particularly when there are many API intermediates.

i. One way to guard against this is to stage the API process to produce key intermediates which are made in surplus as a contingency.

3. **Phase 2b API Supplier**. Since the old API CMO is not a commercial manufacturer, and really NOT a viable candidate for Phase 3, you must change API source before Phase 3, at least, and choose a commercial supplier for Phase 3.

The question to resolve is whether to change the manufacturer <u>before</u> production of Phase 2b -- and have continuity of supplier for both Phase 2 and 3, <u>or</u> to make Phase 2b at the old CMO and make Phase 3 at the potential commercial manufacturer.

i. Since progress on trial development depends on timely initiation of Phase 2b, risk of delay or failure must be evaluated for each of these two options. Since these risks are significant, senior management must be made aware of them and buy into the decision.

b) Delays associated with technology transfer/occupancy would make it impossible to make Phase 2b at CMOs A-C and keep the clinical trial program on track, even apart from the risk of an unexpected result associated with the site change.

i. Equipment these CMOs would use for Phase 3 is at least 20X scale and therefore not appropriate for either the process studies to define the new PM I process or Phase 2b material. Therefore, you would first have to make some sort of scale trial at these contractors to "demonstrate" the process.

c) Least risky solution is to source API for Phase 2b at old CMO and prepare new CMO for Phase 3. Risk of failure and delay with old CMO is low and equipment is the proper size (2 kg/batch) for Phase 2b as well as for process studies on control of polymorph.

i. Downside is you must scrupulously establish equivalency between Phase 2b and Phase 3 API and Drug to avoid the risk of a Phase 3 trial result different from Phase 2b due to the source change. Although this equivalency would also need to be established if you went to a new contractor for production of both CT materials, the risk of non-equivalency MAY be smaller if you switch early since the site would be the same.

d) You must resolve quality issues at the old CMO and ensure aspects of the production are in compliance with Q7a.

e) You must manage the scaleup and technology transfer of the new API process to the new CMO with plenty of time to spare. The preparations to transfer technology to the new CMO must proceed concurrently with the Phase 2b production. The new CMO will need 2-3 months for the CMO to confirm process and methods internally before preparing to run.

4. **Drug Supply**. You must demonstrate control of the PM state during production of the Drug Product as well as use the opportunity to perform additional effect of variable studies to establish compliance with the principles of ICH Q8. Keep in mind the FDA's "life cycle" approach to process validation. The earlier key data are collected, the more solid you support for your design space.

   a) For this production, you will make about 26k tablets to cover the defined clinical trial load of 18k tablets. You should collect a lot of data, including data on API losses in the process, to prepare for scaleup.

   b) After production of the required clinical trial supplies, you will need to evaluate scaleup issues in preparation of the Phase 3 production.

      i. You can use the extra API produced for some of these studies. You will need extra API from the Phase 3 production to complete the scale studies for the drug process prior to actual drug production

5. **Stability and equivalence studies** are going to be a critical benchmark for you to establish correspondence -- both forwards (into Phase 3) and backwards (to Phase 2a) -- that the quality, identity, purity and efficacy of the Drug Product are not diminished by the process and materials changes.

   a) Equivalency must be established whenever any significant change occurs in the API (or Drug) Process by accelerated stability testing and analysis beyond specification tests, including bioequivalence. Change in manufacturing site or scale, source of critical raw materials, or process conditions which control a CTQ attribute are significant changes where equivalency should be established.

   b) You should perform formal risk assessment before every significant process change, to ensure you have identified every element that can make a difference. QA investigations required by loss of control are expensive, resource intensive and can introduce significant delays that are hard to recover from.

   c) Ensure all excipient are commercial materials sourced from the supplier you intend to use commercially. This minimizes introducing this risk into the Phase 3 production. Begin the evaluation of security of supply chain and quality of suppliers.

Phase 3 Program

1. **API Supply**: You should include overages for issues related to supply chain, patient washouts and changes in patient numbers, as well as compassionate use. Quantities to make could be the following:

   a) Clinical Trial (CT) requirements for Phase 3 -- 750 PTs @ 6 months treatment = 2X Phase 2b. When the trial contingency is added, this comes to 30 kg API as Drug.

      i. Trial requirements (30 kg) plus losses and contingency 35% to account for wider compassionate use requirements brings total to about 54 kg.

      ii. Plan to produce 3 API batches to demonstrate control of process and API quality on commercial scale, preparatory to process validation. Total amount depends on batch size appropriate for CMO's equipment and the increased API requirements for formulation process studies in the larger equipment.

2. **Commercial CMO Selection**. Based on the QA audits and your investigation into the three CMOs, you created the following risk/benefit matrix

CMO	Benefits	Risks/Issues	Strategy
A	1. Good compliance history and immediate experience with this chemistry, API production and cytotoxic materials. 2. Equipment is large enough for launch and is readily available. 3. Willing to discount in return for "launch + 2" commitment. 4. Planning expansion of cytotoxic suite which will raise capacity. 5. Best chance of passing a PAI with no significant issues.	1. No particular strength in technology or starting materials, thus limiting longer term cost reduction 2. Requires immediate commitment. 3. Without expansion or alternate supplier, production is limited to about 900 kg/yr, which will likely be below target if launch is a success. 4. Will require capital (M$1) for suite expansion to 60 kg/batch.	Use for Phase 3 production and to study effects of variables and validate process
B	1. Initial quote is lower cost than and may be more room for price negotiation because of cultural issues related to negotiation. 2. Basic in starting materials means good strategic and cost situation 3. Making APIs currently so control of cross-contamination is already in place. 4. Eager to get into US market and willing to make required compliance changes.	1. Compliance is weak and cytotoxic controls need facility modifications. At this point, they cannot pass even a supplier qualification audit. 2. Parent company has a negative "history"; however, API facility has no specific problems. 3. May be less willing to cooperate when extent and cost of changes needed for compliance becomes apparent.	Starting materials from this company should be used in at least one batch of the Phase 3 production if the SM can be qualified. Set up as an alternate API supplier provided they can make necessary changes to Quality system.
C	1. Very good long term potential for strategic defense against generics because of patent. 2. Company has sound technology and infrastructure and has own R&D lab to support improvements. 3. Major Pharma have already recognized the CRO arm as good economy -- may encourage their management to support modernization of the facility. 4. Facility capacity is larger and uses more economical starting materials.	1. Compliance is weak and business has not been focused on production of pharmaceuticals. Very risky. 2. Facility modifications needed to establish cross-contamination and isolation controls needed. They may require capital from you. 3. Your negotiating position with them is weak because of their strong IP position and because your company does not represent a near term prospect for cash business	If positive Phase 3 results, they may be open to some kind of profit sharing in return for license to their technology. Evaluate if your process studies gives you the opportunity to establish a process patent for the polymorphs since their patent does not disclose such an invention.

a) CMO A represents minimal risk and the least uncertainty with respect to technology transfer and compliance, particularly since you were able to negotiate a cost reduction by commitment to produce "launch plus 2" year volumes there.

   i. CMOs B and C represent equivalent risk/benefits, depending on how things develop. You should pursue both until the longer term viability of one versus the other becomes apparent.

   ii. CMO C represents the best long-term option if you can negotiate good conditions.

3. **Development Studies** will need to verify that the API and drug processes can be validated successfully and that all necessary process and quality controls are in place. Where possible, quality should be controlled by process monitoring rather than only by analysis of the products. Much of this work would have been conformed in conjunction with the Phase 2 program (see above). These would include:

   a) One of the most critical tasks is the effects of variable studies for API and Drug manufacturing processes to ensure scale and quality related effects have been well-understood and controlled.

      i. The API process is being scaled up by a factor of 20 for the Phase 3 equipment, even though the actual batch size will be only a factor of 13.

         - This size of a scale-up can be very significant with respect to wall effects, localized concentration effects, and accurate control of homogeneity and thermodynamics.
         - Data should be collected which confirms the assessment of scale-related parameters to ensure these points are properly supported in the development and manufacturing process section of the NDA.

      ii. The Drug process is being scaled up by similar factor - to 300 ktab/batch. Control of the mixing and homogeneity of the wet granulation process will be critical to ensure good quality granules are produced and PM I is not converted to PM II. An opportunity for PAT!

         - It should be remembered that devices which put energy into the manufacturing process, such as high shear mixers, rollers, and tablet presses, can produce significant heat effects.
         - Data should be collected which confirms the assessment of scale-related parameters to ensure these points are properly supported in the development and manufacturing process section of the NDA.

   b) Evaluating API made from commercial starting materials and raw materials. This evaluation should include API made from alternate starting materials -- CMO B -- and supply sources to establish flexibility of supply and also identify parameters which could impact quality which do not reveal themselves until alternate suppliers are evaluated.

      i. With no experience in the starting material from CMO B, it would be very risky to make a commitment. The weakness in their quality system there would make any sample, or even sizeable production quantity, subject to variance in manufacturing conditions.

   c) Confirming all excipients used in drug product have monographs or can be justified.

   d) Auditing suppliers and verifying security of supply chain.

e) A strategy for process and facility qualification and validation should be established prior to Phase 3. Strategy should identify which elements will be performed at which point in the product development cycle, keeping in mind the principles in the FDA's draft guidance on process validation. This ensures cost and resources for qualification activities are expended in a manner consistent with their technical and regulatory value.

f) Stability studies should cover ALL expected commercial supply and production conditions, including packaging, extended intermediate holds and/or transport, etc.

g) Options for backup supply and second source can be evaluated and necessary studies performed after the Phase 3 production is complete.

4. **API and Drug Production for Phase 3** should cover the development and commercial aspects already described above. Three batches of each should be performed, but all three batches do not need to be performed at once. For the purposes of this exercise, however, it is assumed that they are.

    i. Expect to produce at least 80 kg. API, which is 3 batches at 67% commercial batch size.

    ii. Expect to produce about 600 ktab in 3 batches which is 67% of the commercial batch size.

b) Compliance issues at both manufacturers should be addressed before Phase 3 production and a Quality Agreement should be in place. Supply contract should also contain compliance provisions.

c) Stability studies should start promptly to ensure timely data are available for NDA submission.

d) The commercial process development reports should be written after data from the Phase 3 production becomes available.

5. **A milestone plan and budget** is provided on the following page.

Conceptual Layout of Solution to API Sourcing Problem

Task		Issues to Resolve	Cost	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan
Resolve Polymorph Issue	1.	Select Materials Evaluation Vendor & run program	$150																	
	2.	Investigate API at old toller, define new process	$100																	
	3.	Establish new stability indicating analytical methods for API and Drug																		
	4.	Evaluate drug process using old API.	$15																	
	5.	Process Demonstration Run for PM I API.	$130																	
Clinical Trial Production - Phase 2b	1.	Define Clinical Trial requirements for Phase 2b and 3, including contingencies																		
	2.	Production of Phase 2b API process & release.	$260																	
	3.	Start normal/accelerated stability studies for API										D	D		D	D		D	D	
	4.	Production of Phase 2b Drug Product demonstrating new process and release	$20																	
	5.	Normal/accelerated stability studies for Drug Product												D			D			D
	6.	Clinical Trial Packaging & Distribution	$50																	
Other R&D	1.	Define API and Drug requirements for development work required to as per ICH Q8.																		
	2.	Complete development of all Methods of Analysis and write development reports																		
	3.	Evaluate raw materials suppliers, including the starting materials. Confirm quality and security of supply chain. Audit critical suppliers.																		
	4.	Validate analytical methods																		
	5.	Define process validation strategy -- identifying which paramaters are needed before Phase 3 and which can be done after Phase 3 results																		
	6.	Perform Effects of Variables studies for API manufacturing process at old toller, particularly with respect to scale issues	$175																	
	7.	Perform Effects of Variables studies for Drug Product manufacturing process , particularly with respect to scale issues	$200																	
	8.	Define Critical Quality parameters and process controls for commercial processes																		
	9.	Write process development reports																		
	10.	Perform equivalency studies for API/Drug from different sources																		
	11.	Qualify backup suppliers, establish stability.																		
API Toller Selection & Setup	1.	Evaluate technical capabilities and risks associated with each toller option and renegotiate proposals																		
	2.	Define cytotoxic requirements for API process																		
	3.	Conduct toller audits																		
	4.	Define overall manufacturing strategy, including primary and secondary supply of API starting materials and API																		
	5.	Select Toller & negotiate contracts																		
	6.	Technology Transfer and Validation																		
	7.	Toller internal evaluation of process and methods																		
	8.	Qualification of tollers' starting and raw materials and supply chain validation																		
	9.	Qualification of Vendor's API Material																		
	10.	Quality and Hazard Reviews, equipment preparation and qualificaiton	$100																	
	10.	Facility verification and preparation of quality documention and Master Production Records																		
	11.	Qualification of alternate API sources																		
Clinical Trial Production for Phase 3	1.	Production and release of Phase 3 API (80 kg)	$3,100																	
	2.	Initiation of normal/accelerated stability studies for API to establish commercial retest date																		
	3.	Production and Release of Phase 3 Drug Product	$450																	
	4.	Initiation of normal/accelerated stability studies for Drug to establish commercial shelf life																		
	5.	Clinical Trial Packaging & Distribution	$200																	
		PROGRAM TOTAL	**$4,950**																	

D Stability data available to verify program

Production activities

Critical demonstration studies

Biotech Company API Sourcing CMC Workshop

API REQUIREMENT/PATIENT		
Tablet	0.100 gm API	
Dosing, P2	200 mg/day, 28 days, 3 cycles	
Dosing P3	200 mg/day, 28 days, 6 cycles	
Quantity per PT/Q	16.8 gm	168 tablets/3 cycles
Inventory/trial loss	15%	
Deliver	19.8 gm	198 tablets
Allow for Phase 2b (gm)	20.0	
Allow for Phase 3 (gm)	40.0	

Volume Estimates (kg) for Production of API for Clinical Trials								
Drug Arm in Trials		**Deliver (kg)**	**kTab**	**Loss**	**Contingency**	**Allow**	**Extra API**	**Make**
Phase 2 (PTs)	90	1.80	18.00	15%	20%	2.65	3.00	6.00
Phase 3 (PTs)	750	30.00	300.0	15%	35%	54.30	20.00	80.00

Notes

1. **Processing losses cover API loss during formulation**
2. **Contingency is extra drug made for patient flexibility, compassionate use, or potenial shipment damage**
3. **Extra API for process studies and tox, ADME work. Extra API for P3 to allow production of a 3rd batch for stability.**

Launch volume & market		
PTs	100,000	(Orphan Drug = < 200k PT)
gm/PT/yr	55	(three 3 month treatments)
	35%	patient loss
kg/yr	3,604	market. Launch 500 kg.

API PRODUCTION INFORMATION

API Prod Volume (kg)	API Cost $/kg	Batch Information			Total Cost (k$)	Batch Size	Scaleup From 2b
		Max (kg)	Number	Size (kg)			
Program Cost Using Old CMO & CMO A at discounted price.							
6.00	$65,000	2	2	3.00	$390	2.00	
80.00	$38,000	40	3	26.67	$3,040	26.67	13
					$3,430		
Program Cost Using Old CMO & CMO B							
80.00	$40,000	50	3	26.67	$3,200		
					$3,590	**P3 as % of commercial**	
Launch Production						**67%**	
525.00	$38,000	40	13	40.38	$19,950	40.00	20

DRUG PRODUCTION INFORMATION

Starting API (kg)	API Loss (%)	Production (kTab)	Tableting & Packaging			Drug Cost (k$)	Program Cost	Batch Size	Scaleup From 2b
			Placebo	$/AI tablet	$/kg API				
3.00	15%	25.5	$0.75	$8.40	$83,971	$19.1	$409	12.50	
70.00	15%	595.0	$0.75	$5.22	$52,206	$446	$3,486	233	19
						$465	**$3,895**	**P3 as % of commercial**	
Launch Production								**67%**	
525.00	4%	5,040	$0.75	$4.71	$47,083	$3,780	$23,730	350	28