Client Information Pack

Voice of the Client
Global Service Excellence

Welcome and thank you for choosing

Patheon
Performance the World Over®

We are the leading provider of drug development and manufacturing services working with global pharmaceutical, biotechnology and specialty companies.

By choosing Patheon, our extensive global network and expertise can be leveraged to support your goals and, our teams will seek to provide service and technical excellence.

This brochure aims to explain:

- How Pharmaceutical Development Services (PDS) works.
- The process of initiating project development activities at Patheon.
- The information we will require from you.

Should you have any questions regarding this process please contact your Project Manager or our Voice of the Client Program Director:

Beth Marshall
Voice of the Client Program Director
+44 (0) 7921 485146 - cell
Beth.marshall@patheon.com

Your Team

Once the scope of your project is agreed and the contract has been signed by both parties, your Project Manager (PM) will be assigned. The PM will then work with relevant Sales and Quotes representatives to ensure effective handover of all business intelligence and client technical information to the project team.

Your PM is the leader of the internal project team, they are your 'go to' person, responsible for co-ordinating activities within Patheon, managing the project timelines, providing you with project updates and managing the business aspects of the project including invoicing and project scope changes.

Core Team
Client Team Members
Project managers
Analytical Development
Pharmaceutics / Manufacturing

Extended Team	
QA Complience	Microbiology
Planning	Quality Control
EH&S	Commercial Operations
Supply Chain	Business Management
Packaging	Sales
Engineering	Finance

Continues

Core Team

Patheon project teams comprise of project leader, core team members, extended team members and client representatives.

Project Leader: Project Manager is the appointed project leader responsible for leading the PDS Project team to facilitate agreement to how the project will be executed within Patheon.

Core Team Member: A single representative from primary functional areas who takes full responsibility for all project activities executed in that functional area. Responsibilities include:

- Design and execution of project activities to agreed timelines.
- Identification, monitoring and mitigation of identified project risks and issues and escalation of issues as appropriate.
- Critical evaluation of all scientific data including appropriate follow-up actions, recommendations, etc., in line with project objective and strategy.
- Local scheduling of all assigned project activities as appropriate.
- Interaction with appropriate support functions and related outside vendors and contractors.
- Timely communication of progress, issues and performance to budget to the Project Manager and the team, either formally (meetings) or informally, as appropriate.

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Extended Team Member: Representatives from required support groups.

- Extended Team members operate under the direction of the Project Manager or responsible project core team member.
- The responsibilities detailed within the Core Team Member section also applies to Extended Team Members.
- Meeting attendance requirements etc. will be agreed with the Project Manager in line with the timing and scope of associated activities.

Extended Team Member Roles:

- **Microbiology/QC Labs** – Developing, testing, validating and transferring analytical and microbiological test methods for raw materials and finished products.
- **Quality Assurance (QA)** – Quality support on all batches manufactured. Regulatory Affairs personnel are available for consultation at the client's request.
- **Materials Management** – Purchasing, inventory control and production planning of all batches prior to Process Validation.
- **Business Management** – Project leadership post-Process Validation.
- **Environmental Health & Safety** – Toxicity classification assessments, process safety evaluation and handling guidelines, air assessments and medical review for special precautions.
- **Sales – Account Executives** – Liaising with clients to evaluate new business opportunities, interact with the Quotations business unit in the Request For Proposal (RFP) process and with

Continues

Project Managers in the processing of Project Expansions.

- **Operations and Production:** Management of site operations and production equipment and personnel for commercial and GMP activities
- **Planning:** Planning and scheduling production orders for commercial and GMP activities and resources. They also evaluate production readiness.

Site Visits – Come and See Us!

Whether you wish have a face to face team meeting or observe the manufacture of your product, we look forward to hosting you! Please contact your project manager to arrange a visit, they will make the necessary arrangements and ensure your stay is enjoyable and we are prepared for your arrival at the site.

If you are entering a manufacturing area, we will arrange any necessary GMP briefings or EH&S activities such as the fitting or use of safety equipment as necessary. You will always be accompanied to and from the Operations areas while on site.

Making you comfortable:

We will seek to help make your stay comfortable. Your project manager will connect you with a resource at the site that can assist with arrangements and will provide a brochure listing recommended hotel accommodations, limo services, restaurants, etc. Special dietary requirements should be communicated in advance if possible.

The Kick-Off Meeting

An on-site kick off meeting is the ideal opportunity for you meet your team, familiarise yourself with the facility and it allows your team to better understand your expectations and goals. If an on-site kick off is not possible, your PM will arrange a teleconference with your team representatives and all relevant Patheon functions.

We want a smooth start so our goals in the Kick-Off Meeting include:

- An introduction to you and your project – history, indication, goals including submission filing plans, market, etc.
- An introduction to the Patheon team.
- QA agreement requirements, EH&S Categorization, MSDS requirements
- API availability and vendor, special conditions, shipping requirements
- Review proposal and technical package in detail including:
  - Analytical development
  - Microbial limit test method
  - Formulation development
  - Stability (program, conditions, go/no go decisions)
  - Manufacturing/packaging
  - Proposed Timeline
- Discuss business management processes including Change of Scope, Purchase Order requirements, billing preferences, etc.
- Identification of key decision makers for critical aspects of the project.
- Agree the routine communication plan.
- Establish critical milestones.
- Introduce you to Patheon's Voice of the Client Program which supports routine

Prior to Kick Off, the Project Manager will liaise with the Account Executive and client to ensure the team have all the information required to move the project forward.

Project Start up Requirements

- Introduce Furnished API Import Routing Guide. This includes information such as: Product storage/shipping conditions, API value, Manufacturer's C of A, IND #, FDA registration # and/or USDA # from Client.
- Obtain Manufacturer Name, Manufacturer Site Address, Specifications, C of A, MSDS, Animal Contact Letter (BSE/TSE), Allergen Letter, OVI/Residual Solvent Letter and Kosher Letter for API and furnished goods from Client.
- Introduce Cleaning Validation Information Sheet to Client for completion
- Request Reference Standards and impurities for Analytical Development.
- Introduce Micro Limit Test Memo
- Obtain API GMP certificate for MLT

Requirements may differ depending on phase or scope however; we provide check lists of the information required from you. See the Advance Information Section for the detailed checklist.

Managing Changes to your Project Requirements

Changes to the Project Scope or Project Expansions:

Change of Scopes (COS)

It is quite usual during the lifecycle of a project that the scope will evolve and additional items are required or aspects of the project are not required from the original proposal. We handle these occurrences through our change of scope process. A change of scope can also be used to alter project deposits or to change other legal terms. The original proposal number is retained and is managed by changing the COS number throughout the project lifecycle.

The Project Manager will work with the client in the agreement of the change of scope and will manage the communication process with the client:

- COS is initiated once the additional activities are identified and agreed
- The scope of technical activities is agreed upfront before the COS is generated
- COS progress is detailed into the Meeting Minutes and Action Items
- Once the COS is issued, the Project Manager will inform the client about the content, work and expected approval timelines.

Project Expansions (PE)

Project expansions are another means to generate proposals and are used for new development efforts, changes of clinical phases (phase 11 to 111) and to avoid a long string of COS stretching over multiple years. The Quotations team will work with the Project manager and Client to scope out the required work and provide the required proposal and cost estimate. A new quotation number is generated to track this approach.

Material Management and Shipping

At Patheon, we carry a comprehensive inventory of standard excipient materials and packaging components from assured suppliers. Where possible, we encourage clients to use Patheon standard materials as it removes the need for any additional supplier assurance or additional procurement activities. This helps in terms of speed and cost when starting a project.

Where we need to use non-standard excipients and packaging components the cost of procurement in compliance with Regulatory requirements is billed back to the client.

Please ask your PM regarding lead times for procurement of specific standard materials and components. A 4 to 6 week time-frame is usual.

Active Pharmaceutical Ingredients (APIs)

Patheon does not source Active Pharmaceutical Ingredients (APIs) for development projects and you will need to supply this in the agreed upon standard lead time for furnished materials good time (typically 21 days). Please notify your PM before arranging shipment and ensure the API is accompanied by Certificates of Analysis (COAs) from the API manufacturer including confirmatory results if applicable.

Non-GMP Materials

The manufacturing of non-clinical development material is generally conducted under non-GMP conditions in the Pharmaceutical Process Technology (PPT) area. Non-GMP API and excipient samples from vendor(s) can be used for development batches however, all materials to be used for development batches must have a CoA and BSE/TSE letter at minimum.

GMP Materials

To ensure a successful and efficient start to GMP activities all client supplied materials must be received on-site 3 weeks prior to manufacturing start date to ensure adequate time for sampling, testing and release.

If there are delays in receipt, Patheon will work with the client and internal groups to evaluate impact and assess if production can proceed as scheduled.

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Material Management and Shipping

Receiving Materials

To avoid issues and delays, all shipments should be accompanied with a CoA, a BSE/TSE declaration letter and a Material Safety Data Sheet (MSDS).

Please send a pre-alert e-mail containing a copy of the shipping documents to the attention of the Project Manager. A Patheon Purchase Order number will be generated and supplied by the Project Manager.

Shipping Materials:

Patheon has a primary carrier and the use of other carriers should be communicated to the Project Manager as early as possible to allow us to obtain the necessary information.

Additional information required from the client include:

- Who will be the Importer of Record? I.e. who will be paying duties/taxes and freight costs?
- IND number and/or FDA number, if applicable.
- HTS Code: Patheon's Logistic group can assist if required.

Note: If temperature monitors are required for the shipment of Finished Goods, these would be supplied by the client or carrier. ■

Manufacturing and Packaging Preparation

Ensuring we have everything in place to support your development or clinical timeline is critical. We therefore work to get everything in place to allow us to schedule and execute the manufacturing or packaging activities.

Non-GMP Manufacturing

Non-clinical manufacturing activities such as small scale prototypes, feasibility and scale-up batches are usually conducted under non-GMP conditions in the Pharmaceutical Process Technology (PPT) area.

For activities in the non-GMP area:

- Non-GMP API and excipient samples from vendor(s) can be used for development batches
- All materials to be used for development batches must have a CoA and BSE/TSE letter at minimum to be allowed for non-GMP production usage
- It is usual for a cleaning residual assay method to be required prior to using API for development manufacturing.
- Work instructions, in-process physical testing results and observations are documented in lab notebooks or technical Batch Manufacturing Records (BMRs) (not QA approved)
- PPT Technical Project Lead will be responsible for scheduling the development batches if the PPT lab is designated as the manufacturing area.

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Manufacturing and Packaging Preparation

GMP Manufacturing

To ensure a successful and efficient start to GMP manufacturing and/or packaging, the following items should be addressed as early as possible.

- It is recommended to provide at least a 45 day lead time for notification of production orders.
- API, excipients, packaging components to be received on-site 3 weeks prior to manufacturing start date to ensure adequate time for sampling, testing and release.
- Readiness checks are carried out 7 days prior to planned manufacture date:
  - All raw materials, API and packaging components released
  - Batch Manufacturing Records (BMRs) and/or Packaging Work Orders (PWO) approved internally and by the client.
  - Finished product sampling requirements to be completed and approved internally and by the client.

If there are delays to any of the above listed items, Patheon will work with the client and internal groups to evaluate impact to order readiness and assess if production can proceed as scheduled. ■

Project Closure and Transfer

When a project is cancelled or terminated, the Project Manager will work with you to close out the following requirements:

- Discuss any outstanding items, materials or equipment and determine final strategy/timing for closure
- Set up a lessons learned/project closure meeting, if applicable (see below).
- Prepare a Change Control to obsolete any Patheon product codes, excipient codes or other related documentation in the manufacturing and analytical area.
- Request a Material Disposition Report for materials that can be destroyed
- Complete Project Closure form and obtain approval from Client
- Obtain decision/ship arrangements on outstanding Stability samples, Reference Standards Return remaining materials, products or samples to the Client
- Return or retain any dedicated equipment or tooling as per Client's instructions
- Send a notice to Finance to request Deposit return (if applicable)

Lessons Learned Program

Throughout each project life cycle, lessons are learned and opportunities for improvement are discovered. As part of a continuous improvement process, documenting lessons learned helps the project team:

- Discover root causes of problems that occurred
- Mitigate or prevent project risks
- Celebrate project successes
- Share best practices across the Global Patheon.

The learning's are documented and retained in a central repository and can be reviewed by the project team during the initiation of a new project with the client to minimise the chances of any repetition of any issues.

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Project Transfer & Closure

Technical Leadership

Client Service & Issue Escalation

Advance Information Checklist

Project Closure and Transfer

Transfer from Development to Commercial

We routinely support the transfer of client products from development to commercial scale lines within the Patheon network. Your PDS team would work closely with the Commercial technical team to support a successful transfer of product.

A Technical Transfer Project Leader and Commercial Business Manager will be assigned to the project who will work closely with the Project Manager and project team to transfer all the relevant knowledge and expertise.

The Project Manager, Business Manager and technical transfer project leader will work together to ensure a smooth transfer of the project by:

- Collecting all the available technical information
- Initiating or reviewing Commercial Quality Agreements and Commercials Proposals
- Evaluating the product feasibility
- Evaluating the suitable timelines
- Understand forecast requirements and build into Business review model
- Review and implement validation requirements
- Prepare for Pre-Approval inspection

Once the project is transferred, the technical transfer project lead will build an appropriate Commercial project team in order to plan and manage all the project activities directly with the client. ■

Technical Leadership

PDS have extensive experience and expertise both locally and globally.

Our Pharmaceutical Development Scientific Teams are led globally by:

Anil Kane, Ph.D., MBA

Executive Director, Global Formulation Sciences, PDS

Dr. Kane has more than 25 years of experience in the science and business of taking molecules through the entire drug development process. His extensive knowledge spans early stage development to scale-up and commercial manufacturing, and includes technical transfers between global sites and drug lifecycle management. +

William E. Weiser, Ph.D.

Global Head, PDS Analytical Sciences

Dr. Weiser is an expert in analytical method development and validation for APIs and drug products. His expertise includes stability program development, analytical method troubleshooting, preparation of the CMC Section of IND/NDA/CTD submissions, and U.S. agency for European API manufacturers.

Additional expertise includes:

Kaspar van den Dries, Ph.D.

Director, R&D Europe

Dr. van den Dries is an expert in the formulation of poorly soluble compounds and self-emulsifying drug delivery systems with experience spanning the entire solid dose form development cycle.

Roman Hlodan, Ph.D.

Biopharmaceutical Specialist

Dr. Hlodan is an expert in the development of biopharmaceuticals, including analytical method development and validation, stability program management, and formulation development.

Geoff Carr, Ph.D.

Director, Analytical Development

Dr. Carr's expertise includes the development and validation of analytical methods, use of spectroscopic techniques to identify impurities, specification development for APIs and drug products design, API characterization, drug degradation chemistry, and management of stability programs.

Stefano Chiaramonti, Ph.D.

Group Director of Operations, PDS

With 17 years of experience in pharmaceutical development and operations leadership in Europe, and as a certified Qualified Person (QP), Dr. Chiaramonti is an expert in quality and EU regulatory requirements.

Paul Sabo, Ph.D.

Senior Formulation Specialist

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Technical Leadership

Client Service & Issue Escalation

Advance Information Checklist

Voice of the Client (VOC) NPS and Issue Escalation

Patheon's Voice of the Client Program has two primary functions.

- To ensure the client has a voice within Patheon through the VOC Client Feedback Process which is based upon the Net Promoter System®.
- To manage client issue escalation, ensuring visibility and support for any critical issue impacting our clients.

Client Feedback:

We ask our clients to support VOC by completing a 5 minute survey, 3 to 4 times a year. This is 15 minutes invested in your service experience.

Every survey is reviewed at a senior level and you will always get a response. Our objective is to understand and respond to your needs thus improving your service experience. The feedback is also used to recognise our staff for service excellence.

- We look ahead: Surveys are usually scheduled in advance giving you clear visibility of the timing and the opportunity to talk through the process.
- We value your time: We limit questions, ensuring every survey is short and will only take approximately 5 minutes to complete.
- We give you access: You have access to all levels of the organization. If you wish to talk to someone outside the team, you will be provided with escalation contacts by your Project Manager. We are all here to help!
- We want to listen: Feedback is managed and communicated with the sole purpose of improving the service we provide.

Escalation:

If there are issues, we want to ensure you have the right support. We therefore provide clear site and above site escalation routes for you to use should this be needed.

We also have a Global Issue Escalation Process across both Commercial and PDS which ensures there is the necessary visibility and support to drive resolution.

Please talk to your Project Manager about escalation routes or contact the VOC team on client.services@patheon.com. ■

Advance Information Section

	Item	Client	Comments
Environmental Health & Safety			
1.1	Complete questionnaire	x	
1.2	Provide MSDS	x	
1.3	Provide toxicity data	x	
1.5	Provide API explosivity data (MIE & Kst).	x	
Materials			
API			
2.1.1	Provide manufacturer CoA and/or Client CoA	x	CoA must include storage conditions, expiry date and retest date.
2.1.2	Provide documentation for New Part Set -Up	x	The following documents are required to receive material in the GMP warehouse. o Testing specifications o MSDS o OVI/Residual solvents statement o BSE/TSE statement o Letter stating GMP status of manufacturer if material is non -compendial o Validated test methods (if non -compendial) o Allergen Letter (if available) o Micro Test Letter (to document justification if Micro testing will not be performed.)
2.1.4	Provide API Characterization / Preformulation Report	x	If available
2.1.5	Provide Import Routing Guide	x	Provide template to Client.
Excipients			
2.2.1	Provide Vendor Specifications/CoAs	x	
Packaging			
2.3.1	Packaging Specifications	x	
Analytical/Micro Methods			
Drug Product Cleaning Residual Method (by LCMS)			
3.1.1	Provide Existing Method & Validation Report	x	
3.1.2	Provide Residual Limit information	x	
3.1.3	Provide 0.5g of each reference standard	x	
	Excipient sample acquisition	x	
3.1.4	Provide API solubility and stability data (if available), structure, molecular weight	x	Where available.
Product Methods			
3.2.1	Provide existing Method & Validation Report for Analytical Methods	x	If available
3.2.2	Provide about 5g of reference standard and CoA		CoA must include st orage conditions, expiry date and retest date.
3.2.3	Order HPLC Columns		Client may supply columns, if available.
Micro Method			
3.3.1	Provide existing Method & Validation & Report		If available
3.3.2	Memo outlining Micro Validation requirements.		
Product Specs			
3.4.1	Provide in -process specs		
3.4.2	Provide release specs (Bulk & Finished Product)		
Manufacturing			
4.1	Provide formulation	x	
4.2	Provide process train	x	
4.3	Provide existing tooling drawing or requirements.	x	
Quality Assurance			
5.1	Perform QA Audit	x	
5.2	Implement QA Agreement	x	BDM/PM to send template to Client.

Voice of the Client

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