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D2.3 Progress report

Search, Match & Connect



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Abbreviations

CBUs	=	Cord Blood Units
GRID	=	Global Registration Identifier for Donors
HLA	=	Human Leukocyte Antigen
WMDA	=	World Marrow Donor Association

1. Introduction to the Search & Match Service

The Search & Match Service is a web-based software application that is accessible through the internet. Since January 1, 2017, the service and database have been operated by the World Marrow Donor Association (WMDA). This service offers users a single comprehensive application that can be used to globally search and provide matches for haematopoietic stem cell volunteer donors and cord blood units (CBUs) while complying with increasing data security regulations. These matches are based on HLA typing of patients and donors/CBUs.

Human leukocyte antigen (HLA) typing is used to match patients and donors for bone marrow or cord blood transplants. HLA are proteins -- or markers -- found on most cells in your body. The immune system uses these markers to recognise which cells belong in the body and which do not.

The Search & Match Service lists over 33 million donors and over 700,000 CBUs from 54 different countries. It allows the opportunity to find a suitable stem cell source as quickly as possible by providing user-friendly interface and functionalities. The probability matching for each donor/CBU is powered by OptiMatch.

OptiMatch is a matching program calculating, for each donor, the probability of the HLA matching at the allele level to the patient. This is based on local population haplotype frequencies in the underlying population. The program was developed by the German registry ZKRD. The first version (October 2006) was based on 3 locus high resolution haplotype frequencies, while the current version (June 2008) is based on 5 locus high resolution haplotype frequencies. The purpose of this algorithm is to find and present a selected list of potential donors and/or CBUs, in which those likely to be an optimal stem cell source for the patient are sorted to the top of the list. Besides the HLA compatibility secondary preference criteria, such as CMV antibody status, gender, and age for example may also be taken into consideration.

In order to improve the data collection, WMDA received an operational grant from the EU to develop an infrastructure that is able to receive and to process larger data sets. When WMDA took over the Search & Match Service it was 13 years old and based on out-dated technology. WMDA initiated a project to fundamentally refresh the Search & Match Service through improving user functionality, increasing the capacity and reliability of data processing and ensuring security and long-term supportability of the solution. The scope of this project also included a desire to receive more data from the WMDA listing organisations (registries and cord blood banks worldwide). For this, the old data submission process was upgraded to be based on an XML (Extensible Markup Language) schema which is considered an industry standard that is extendable, robust and easy to use.

The redevelopment of the Search & Match Service is divided into three phases:

- During phase 1, WMDA modernised the user interface and introduced a predictive matching algorithm (OptiMatch). In February 2017, this new service of Search & Match was launched and has been well received by the community and Search & Match Service users.
- Phase 2 focussed on 'back-end' infrastructure improvements designed to make the overall Service more resilient and performant. A key element of Phase 2 was the demise of the old data submission process and the migration to the new XML data pipeline by which all listing organisations transmit their donor details to WMDA.
- The third phase of development, for Search & Match focusses on improved connectivity, communication and process integration to help ensure that listing organisations have an effective and efficient platform for matching donors to patients. This phase is just commencing and will form one of the main components of WMDA activity in 2019.

The benefits of a new and improved Search, Match & Connect Service

For search coordinators and transplant physicians it is important to have more information available when they are in the process of selecting a donor or a cord blood product. Search coordinators do have a lot of manual work. For example, they type the HLA typing in the software application of their own organisation. They also type the HLA typing in the Search & Match Service of WMDA. After initiating the search, they print the screen and type the HLA typing of the selected donor in an encrypted message to the organization where this donor is listed. If the donor is available a process of fax and e-mail is starting up. The first step to reduce manual work is to create an automated connection to register the patient data directly into the WMDA Search & Match Service. This will take away the first step. The WMDA developed this as a concept and presented it to the WMDA Membership in Minneapolis (USA) in November 2018 ([See video](#)). The membership agreed that this is a step forward. The WMDA is exploring the technical requirements and will launch this mid-2019.

After this first step, WMDA would like to go through the whole search process and take out redundant and manual steps. Some organisations run their software on a legacy system, therefore it takes time to find a solution which is suitable for all organisations.

The following reasons reflect the importance of additional data for the search process for patients in need of a stem cell transplantation:

- The service provides a secure platform to upload and download data files that comply with the European data protection regulations and ISO/IEC 27000:2016;
- The streamlined web-based data upload service gives the listing organisations the possibility to upload data manually or automatically on a daily basis;
- In the past, a search coordinator had to request cord blood unit reports from cord blood banks for relevant cord blood units that are shown on the Search & Match Service. After receipt of all the reports the search coordinator / physician decided if a cord blood unit should be requested for shipment. The new data submission procedure will allow cord blood banks to send all relevant information on cord blood units directly to the Search & Match Service. The search coordinator will this immediately see the details related to the cord blood product in the system. This will accelerate the overall search time and may increase the chance of survival for severe patients.

- The new data submission procedures will provide search coordinators with information on the status and availability of a potential donor. This will help to prevent requests for verification or extended HLA typing from donors that are temporarily unavailable.
- There is an increased chance that the donors and cord blood products of an organisation will be selected when the additional data is provided accordingly.

More information on HLA typing and OptiMatch can be found in Deliverable 2.1 Search algorithm.

2. Project objectives for the period

In 2018, software developers and testers from the WMDA community worked to create the required [XML Schema Definition \(XSD\) files](#). These files define the elements that are allowed in the XML file, the order of these elements and the values that will be accepted. The element names are based upon community specifications and aligns with the European Data Dictionary (known as EMDIS). Several elements are basic elements that should be included in all files, but there are also elements that are specific for donors only or for CBUs only.

This year, two websites of the Search & Match were released:

- <https://dataupload.wmda.info/>, Where registries upload their data / XML migration
- <https://search.wmda.info/login>, To search for a right donor/CBU match for the patient

The project was agile, which means that the project team members had daily stand up calls in order to be sure that the project was delivered in the defined budget and timelines. At the end of the project the infrastructure was tested by a professional company, SQS. This company donated their testing time to WMDA as a gift to the community.

After extensive testing the new infrastructure was ready for launch in May 2018.

In order to be sure that the new infrastructure was capable to process large data files in a timely manner, the decision was taken to ask six organisations to serve as pilot organisation:

- United States, National Marrow Donor Programme
- United Kingdom, Anthony Nolan
- United Kingdom, Bristol Registry
- Germany, ZKRD
- Netherlands, Matchis
- Canada, One Match

These six organisations were selected because of geographical distance (Matchis, Anthony Nolan) and because they have extremely large data files (NMDP, ZKRD). Bristol was selected because of the big amount of cord blood data.

A pilot period of four weeks was scheduled to give the organisations the opportunity to upload their donor and cord blood data in the XML file format. The goal was to process these files in a timely manner. A processing time of 1,5 hours is acceptable for the bigger German file. At the start of the pilot period it took over two days to process the German donor file. This was unacceptable because in total over 100 organisations will upload data files. The queue to process files will be so long, that the data will be shown with a delay to transplant centres and search coordinators.

After the reduction of the processing time, WMDA project team decided to go live. Two environments were created. A staging environment and a production environment. The staging environment is the testing environment. Listing organisations can submit here their first XML file. This is used for testing the XML file and to check if the data are correct. When then file is audited, and the data is correct, the listing organisations gets access to the production environment and can upload their data.

3. Project management

The development was managed by a multi-disciplinary project team, which was responsible for delivering the project within the budget and defined timelines.

The team consisted of a project coordinator (with knowledge about the European GDPR), WMDA business analyst who understands the European organisations, WMDA project manager and a dedicated software team. Based on a request for proposal, that had been sent out to selected software vendors, a collaboration was established with the Bulgarian software company, MentorMate.

3.1 Governance and capacity building

- The Search, Match and Connect pillar is being led by a board committee. The members of this committee are WMDA members from different registries
- The operational manager of the Search, Match & Connect pillar is responsible person for this project and he reports monthly to the Search, Match & Connect board committee to ensure the project fulfils the needs of the members. In June 2018, all WMDA members were updated on the status of the project at the WMDA bi-annual conference in Munich. Regular updates were also provided in the WMDA newsletter which is circulated to all listing organisations each month
- The business analyst from WMDA is appointed as a liaison between the listing organisations and the software team.
- The WMDA software team is responsible for supporting the listing organisations in preparing the XML file and for developing the infrastructure for receiving and processing the XML files.

3.2 Consortium management tasks and achievements

- To reduce the time schedule for uploading and processing donor and cord blood data in the XML file format. The current processing time of 1,5 hours is acceptable for the larger files.
- Migrate all WMDA member organisations from the old DOT20 file to the new XML file. At the moment, 96% of donor data is sent via XML as at December 2018.
- To be able to present the complete donor or cord blood data in a report to transplant centres and search coordinators which reduces the 'time-to-match' for European patients by at least one day.
- Validation of HLA typing is improved for accurate data to transplant centres and search coordinators.
- Provide information about the Accreditation status of a cord blood bank.
- The infrastructure is developed in a way that it can progress two different donor ID numbers, the old one and the global new GRID, see Deliverables D1.1 and D1.2.

3.2.1 Changes in the consortium

Due to personal reasons the business analyst was off for a few months. The tasks were taken over by a project coordinator of WMDA. This had no effect on the outcome of the project.

3.2.2 Problems and envisaged solutions

- The processing time of the XML files was unacceptable, as explained in Chapter 1. This was solved by re-factoring parts of the infrastructure and by speeding up the HLA validation.
- Currently, 18 member organisations (14%) have not migrated from the old format to the new format yet due to different reasons:
 - Some organisations were unable to migrate their donor files but not their cord blood files because the cord blood data are usually stored on paper. This needs to be digitalised first which takes human manpower.
 - Lack of IT resources to modernize the IT infrastructure in the listing organisations
 - Governmental processes are delaying the migration.

WMDA is offering IT and operational support to the listing organisations in need.

- Not all member organisations had sufficient IT resources to migrate timely to the new XML file format. This was solved by adding multi language team members to the WMDA software team.
- In the beginning the data was not correctly presented to transplant centres and search coordinators. This was solved by hiring a testing company and organisation phone calls with the users of the Search & Match Service.

3.3 Dissemination and outreach

- The Search & Match team communicates via Pivotal Tracker, a free agile project management tool used by developers around the world for real-time collaboration around a shared and prioritized backlog.
- The WMDA software team has daily stand-up calls to inform each other about progress and issues
- In April 2018, there was an international meeting in Leiden (NL) to perform the final testing of the new system. The results of this meeting were presented to the Board as recommendation that it should approve the 'go-live' of the new system.
- On WMDA Share the Search & Match Phase 2 Home page was created for the Search & Match team to update the senior manager about the progress of the project.

3.4 Communication between WMDA and the listing organisations

- In 2018, three XML File Processing newsletters were sent out to the IT specialists of the listing member organisations to inform about updates regarding the migration to the new XML file.
- In WMDA newsletters Stem Cell Matters, send out every three weeks, the whole community was informed about the progress regarding this migration.
- At the Spring Meeting in June (Munich, DE) and the November meeting (Minneapolis, USA) the membership was informed about the progress at the time.
- In WMDA Share the [User guide to the Search & Match Service](#) explains in detail the manual steps in the search process. It includes an extensive manual, print screens and a video.

4. Project planning and status 2019

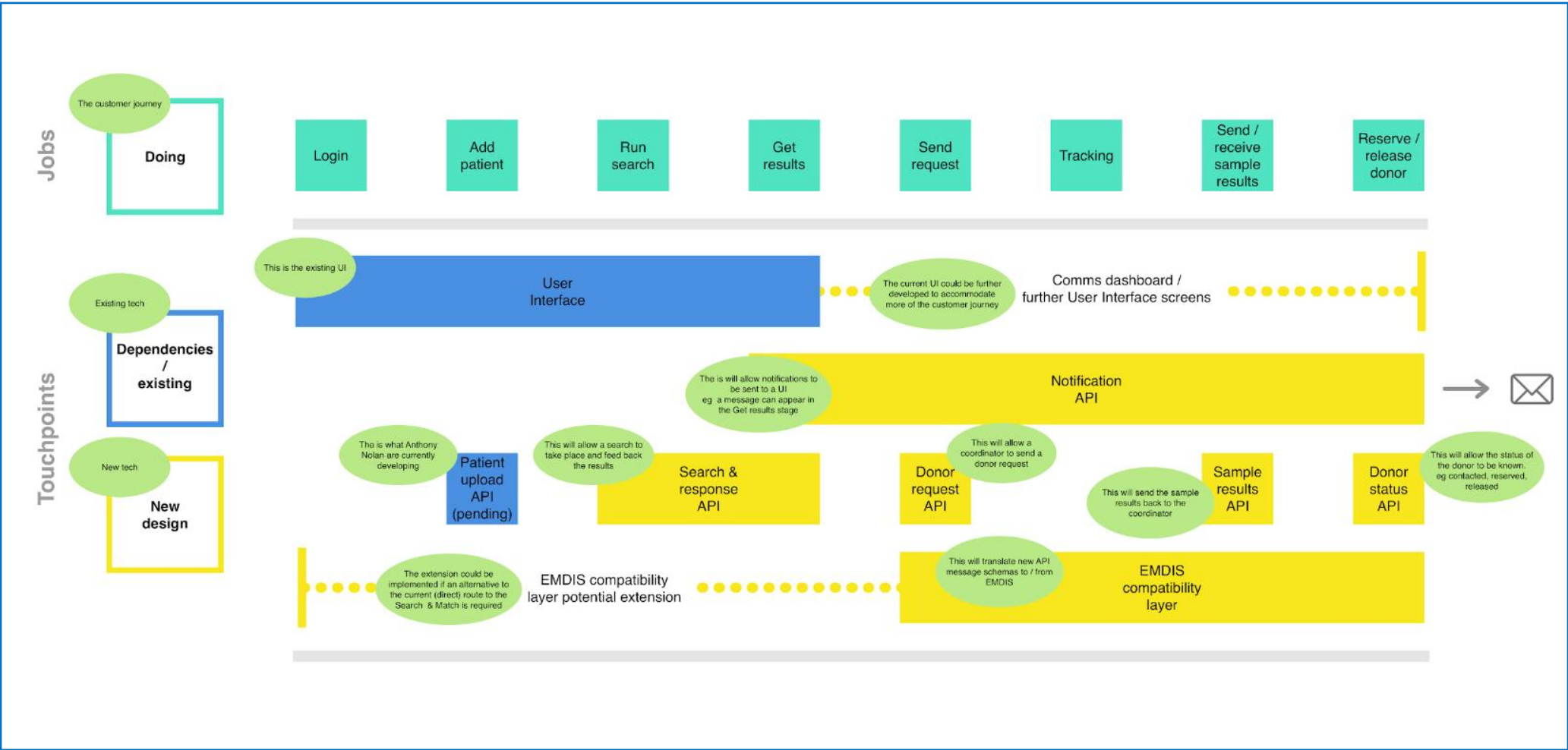
As well as continuing to support migration to XML for the few remaining organisations yet to move across, the primary focus in 2019 for Search, Match and Connect is to implement the next phase of the project.

In the final quarter of 2018, the WMDA management team has spent considerable effort and time working with operational and technical experts from across the WMDA community to define and agree the specific deliverables that will further enhance registry communications. The outcome of this scoping activity has resulted in a clearly defined problem statement: *a registry needs a way to access a complete donor pool and to select and obtain stem cell products out of that pool but...The information is available in different locations, each having its own constraints.*

This next phase of the project will seek to address the problem statement with a vision of delivering an integrated eco-system that democratises search and requests in small and large registries. The WMDA community was consulted on the outline proposal for this next phase during the bi-annual WMDA conference in November. There was overwhelming support – including a majority vote - from the community that WMDA should move forward with this next phase.

In January 2019, WMDA will convene a small core Delivery Team comprised of operational and IT personnel from listing organisations representing both small and large members. This team will be facilitated by a specialist technical design agency to generate a specific project approach and plan for delivery of the concept for this phase which is illustrated in the Figure 1 below:

Figure 1: Search, Match & Connect project blueprint for delivery in 2019



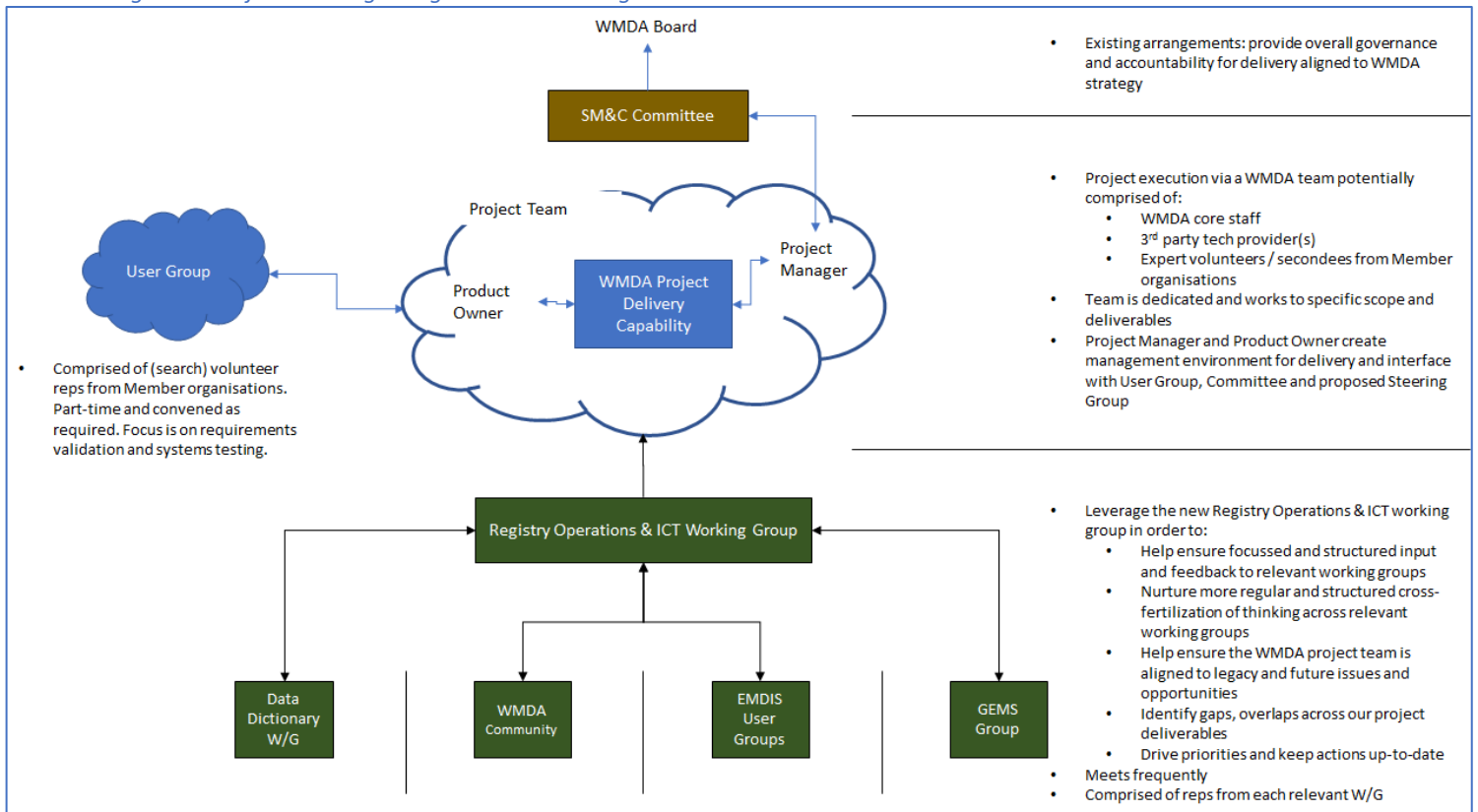
By the end of January, WMDA envisage that the Delivery Team will have a clear and detailed set of planned and prioritised deliverables. These will then form the workplan for delivery of this phase of the project during 2019.

The Delivery Team – and the project overall – will be governed by the WMDA Search, Match & Connect committee in a manner similar to previous phases of the project. It will be driven by a project manager and a product owner who will be responsible for ensuring the requirements and delivery is in-line with community expectations and validated by a User Group that will be made-up from volunteer representatives from a large range of listing organisations.

Depending on the specific project activities that are agreed in January, the Delivery Team is likely to engage the services of one or more specialist technical delivery partners to help with the design, build and implementation of certain deliverables. Such partners will fall under the management control of the Delivery Team project manager and will be sourced in accordance with open procurement processes.

To ensure tight alignment to other WMDA community activities – and to ensure constant and consistent channels of communication – the WMDA Registry Operations & ICT Working Group will provide a regular steer to the project. This Working Group is comprised of experienced community activists from across the world who will provide valuable practical insight and ideas. As always, WMDA will provide regular and transparent progress reporting through Stem Cell Matters and other well used approaches. The proposed working arrangements are summarised in Figure 2, below:

Figure 2. Project working and governance arrangements



The approach to this phase of the project will be a hybrid of traditional waterfall and agile. This is in recognition of the complexity and myriad stakeholders that will be involved in the day-to-day project delivery and the need for clear accountability to the WMDA Board and wider community. Our project manager and Delivery Team are experienced in delivering hybrid projects in this manner.

Whilst WMDA cannot pre-empt the detailed activity plan that is formulated and agreed in January, it is likely that the initial effort will focus on implementation of a Patient Upload API which will benefit members by streamlining process and reducing time to deliver donor matches. Listing organisations have communicated that this is a useful and attractive feature. It is then likely that a range of options will be created to open-up access to tracking functionality for end-to-end donor requesting and reservation regardless of an organisation's size and legacy technical environment.

At the WMDA meeting scheduled for the end of March 2019, the project will be established, and several initial delivery milestones will have been defined.