

ANNUAL REPORT

Technology Transfer Office
Erasmus MC

2015

PREFACE

I am pleasantly surprised with the fresh approach and the clear view on the priorities that the 2015 year report of TTO outlines. The new team has clearly been able to not only open the doors to TTO and become more visible, but also to present impressive growth.

Admittedly, it was not only growth that we were aiming for when we, as the Executive Board of Erasmus MC, decided one and a half years ago to make further investments in TTO: our primary aim involves creating awareness of the importance for valorization and social economic use of results of our great science. And clearly the team of TTO has been very successful in achieving that goal.

Erasmus MC will continue on this road forward in further strengthening its position in the world. However, this will not be achieved if we only focus on top publications, educational primacy and excellence in care. We cannot ignore the potential of promising ideas and results of our employees, which should be further developed into products, services and improved health care for society, as we have described in “Course 18”, our 5-year strategy.

TTO is essential and instrumental for that purpose.

With confidence, I am looking forward to new initiatives that will be initiated and the further development of TTO as a valuable department within Erasmus MC.

Prof. dr. Jaap Verweij, Dean / vice-chairman Erasmus MC



Table of Contents

| | |
|-------------------------------------|----|
| • Introduction | 4 |
| ○ Subsidies and Non-Core activities | 6 |
| • Business Development | 8 |
| ○ Spin-Off companies | 12 |
| ○ Proof-of-Concept Fund | 13 |
| • Legal | 15 |
| • Financials | 19 |
| • Erasmus MC Incubator | 21 |
| • Erasmus MC Holding B.V. | 22 |
| • Outlook 2016 | 24 |
| ○ General | 24 |
| ○ Business Development | 25 |
| ○ Legal | 25 |
| ○ Erasmus MC Incubator | 25 |
| ○ Erasmus MC Holding B.V. | 25 |
| • Personnel ultimo 2015 | 26 |

INTRODUCTION

2015 was the year of first steps into the future based on the new Mission, which we defined and implemented at the end of 2014. We prioritized and focused our activities based on this Mission and we whole-heartedly attempted to execute them with a pro-active and open attitude. First and foremost it has been clear that Technology Transfer Office (TTO) had to pursue and meet with the researchers and clinicians more frequently to create awareness, and to offer the services of TTO in a much more supporting way than before.

TTO's mission statement:

Our Mission is:

- to promote valorization of findings by fostering the interaction of Erasmus MC's inventors with academic institutions, funding organizations and industry,
 - to secure ownership thereof, and
 - to disseminate these findings,
- thereby creating societal exposure, economic value, and income to invest in further research, better education and excellent patient care.

Following the new Mission and the change in attitude, we also changed the way of communication: we proposed to give presentations and lectures at all levels within the organization, which we have done so, as can be seen in Table 1.

Furthermore, we arranged that TTO's offices were officially taken up in the routing of Erasmus MC. With that, our offices are now clearly indicated and easy to find.

Table 1: Communications

| | 2013 | 2014 | 2015 |
|---|-------------|-------------|-------------|
| Internal awareness sessions | 0 | 4 | 34 |
| (Inter)national visits and meetings hosted | 3 | 5 | 7 |
| Networking events | 2 | 5 | 5 |
| Conferences attended | 3 | 2 | 19 |
| (Inter)national Presentations | 0 | 0 | 4 |

Table 1:

Internal awareness sessions: these sessions are essential in our strategy to show what TTO is, and how TTO can add value to the researchers as described in the mission. The 34 sessions have different content and are given at various meetings: from student classroom lectures via research- and departmental meetings, up to a 1,5 hour lecture including break-out case-discussions for the Top-100 managers of Erasmus MC during the Strategy-days. All employees of TTO are involved in these presentations.

International visits and meetings hosted: All of TTO's (inter)national visits and events take place at the Erasmus MC Incubator at the Rotterdam Science Tower (RST). There is a clear wish from international organizations to visit us and to learn how Erasmus MC has set up and manages its Incubator.

In 2015 delegations from Singapore, the Municipality of Rotterdam and the Ministry of Economic Affairs, including the Vice-Minister and the Director-General, visited the Erasmus MC Incubator. Furthermore, we arranged tours in the RST for the management of Port of Rotterdam, the management team of our new Erasmus MC 'Servicebedrijf', Start-up Delta and the Board of directors of Erasmus MC, who visited TTO and the Erasmus Incubator as part of their 'Over de Vloer bij...' tour.

Networking events: As well as awareness sessions, it is also necessary to develop and organize events where scientists, companies, start-ups and governments, who are all key in the valorization process, meet and have the possibility to exchange their views and ideas.

In 2015, two "... Meets Science" conferences were organized ("New Business Meets Science" and "Watertech Meets Science"). Furthermore, the Erasmus MC Incubator also opened its doors during the "Europa Kijkdag", where it was promoted as one of the "Signature Projects of the Year".

Two meet-and-greet lunch events for the companies in the Incubator and for partners in the Rotterdam Science Tower were organized.

Conferences attended: An important activity for TTO is to present and pitch inventions from Erasmus MC at (inter)national conferences. These conferences are important to meet potential Licensees and partners. A good example are the two BIO Europe conferences that we visited in Paris and Munich.

(Inter)national Presentations: TTO was invited to give presentations at the following international events: Licensing Executive Society (LES) Benelux Topic Meeting in Liege (Belgium), the Career Progression Day at IRB Barcelona (Spain), ASTP Proton Annual conference in Istanbul (Turkey), and during a trade mission in Dubai (VAE).

TTO, from its side, has invested in presenting the inventions of Erasmus MC actively on its website and at international conferences. The most important conference in this respect is the BIO Europe, which is organized twice a year and is the place to be to meet and discuss our inventions with key-people from industry and investors.

Together with the Communications Department, we set up a LinkedIn page and created quite some traffic as we post interesting milestones and lighthouse results on a regular basis.

In the last quarter of 2015, we created a short animated movie which summarizes the activities of TTO. In this movie we follow an Erasmus MC employee who has an interesting/exciting innovation. However, he is not sure about the procedures or how to maximize the potential of his invention. After visiting TTO he is supported by our team and brought into contact with the relevant experts who are able to help him further towards valorization of his idea (see our website or <https://www.youtube.com/watch?v=Fflnsxr0nWw>).

We enjoyed the support of the Board of Erasmus MC as they recognize that TTO is instrumental in reaching the goals of “Course 18”, the 5-year strategy of Erasmus MC, and especially with respect to innovation-stimulation and internationalization. Therefore, the Board actively promotes inviting TTO for presentations at all levels, and they also direct researchers and clinicians with innovative ideas to TTO.

With this new collective approach and the reinstated confidence in the role and attitude of TTO, researchers and inventors of Erasmus MC can access TTO more easily. Because of this, the number of requests for support rapidly increased, and as a consequence we had to quickly increase our workforce in order to be able to fulfil all requests. While TTO employed 11,6 FTE by the end of 2014, by the end of 2015 TTO employed 16,5 FTE (both excluding Erasmus MC Holding B.V.).

SUBSIDIES and NON-CORE ACTIVITIES

Although we have defined our Mission clearly, we also decided that all elements linked to the execution of this Mission will continue to be the responsibility of TTO. Therefore we serve as the administrator for several subsidies that need to be carefully administered and have a link to innovations and inventions.

- **WBSO** is a special tax ruling, based on which industrial funding of a project is subject to a tax-reduction. In 2015, the law changed and research institutes such as Erasmus MC would no longer be eligible to receive this subsidy. However, as the interpretation of the law was questionable, we decided to start discussions with the Tax Office. In line with these discussions, we also applied for a subsidy for innovation projects in 2015 (see also Table 4). The definitive amount of subsidy for 2014 (received in 2015) was € 502.745. The discussion with the Tax Office about our application for WBSO 2015 is still ongoing.
- **Octrooifonds** is the Erasmus MC fund for internal investments in Intellectual Property. When an Invention Disclosure (ID) is accepted, is further described in an Invention Disclosure Form (IDF) and finally leads to a Patent Application (see Table 2), the Board funds half of the application costs via the Octrooifonds. When the (granted) patent is licensed, or leads to revenues for Erasmus MC in any other way, this subsidy is refunded. (For details, see our Erasmus MC regulation: “Bescherming en Valorisatie van Intellectueel eigendom van het Erasmus MC” on our website).

- **Licentiefonds** is an administrative Erasmus MC fund for any income (royalties, milestone payments, etc.) related to Intellectual Property (IP) that is currently out-licensed¹. This fund is administrated by TTO but controlled by the Dean. Part of the income has previously been used for special projects, such as funding of the Erasmus MC Incubator.

In 2015, we started a new initiative also financed from the Licentiefonds for Proof of Concept funding under the name UNIIQ. UNIIQ is an initiative at regional level together with Innovation Quarter (the Regional Investment Agency), TUDelft, Leiden University Medical Centre (LUMC) and Erasmus MC. Further details on UNIIQ can be found in a separate section in this annual report.
- **EFRO** is a European subsidy, allocated by the European Fund for Regional Development, used to partly fund the Erasmus MC Incubator in the Rotterdam Science Tower. While the subsidy period ended by the end of 2015, Erasmus MC has the obligation to keep the Incubator running for another 5 years. TTO will continue to execute the management and administration of the Incubator. Over the coming period, TTO will work on creating more awareness for the Incubator and possibly expand its leasable space.

As well as these activities, in 2015 TTO started preparing a new grant application at EFRO for pre-seed funding to close the value chain in the valorization process.
- **Valorization Programme Rotterdam (VPR)** is a consortium of, among others, Erasmus University Rotterdam, InHolland, Hogeschool Rotterdam, Albeda College and Erasmus MC, which runs from 2012 until 2017. The goal of VPR is to disseminate knowledge from the knowledge institutes into the economy and society. The Ministry of Economic Affairs subsidizes the Valorization Programme Rotterdam with €5 million. The activities span the wide range of scouting, screening and valorization of innovations in care.
- **TKI allowance** is a subsidy program initiated by the Netherlands Enterprise Agency (RVO) through the organization Health-Holland to stimulate private-public collaborations. This program will allow scientists to acquire additional funding as well as the contribution of the privately owned collaboration partners. As this program requires a collaboration agreement with an IP clause that is fair for both parties, TTO decided that supporting scientists in the application process increases the rate of success of applications. We actively informed scientists about the existence of the program, screened contracts and advised on how to structure a collaboration to become eligible for the allowance. As we only applied in the last round of TKI, we do not know if additional research funds have been acquired through the TKI allowance.
- **Toekomstfonds** is a credit facility initiated by the Netherlands Enterprise Agency (RVO). Erasmus MC applied for this interest free loan construction. TTO supported the application process.

¹ The term “Intellectual Property” (IP) is used because we collect income not only via royalties on patented technologies, but for instance also on licensed know how and copyrights.

BUSINESS DEVELOPMENT

With the start of a completely new Business Development team at the end of 2014, TTO has developed its Business Development activities on a professional and adequate service level that serves the researchers and clinicians at a very high professional standard.

Table 2 shows a complete overview of the results of Business Development. While 2014 was a start-up year for the “new TTO”, in which we defined and implemented our new work processes, 2015 can be defined as the growth year in which we started to execute on these new foundations.

Table 2: TTO-Business Development KPIs

| Key Performance Indicator | 2013 | 2014 | 2015 | Increase 2014 - 2015 |
|-----------------------------|-------------|-----------|-------------|----------------------|
| Invention Disclosures (IDs) | 40 | 40 | 96 | 140% |
| IDFs Signed | 6 | 12 | 23 | 92% |
| Patent Applications | 9 | 9 | 14 | 56% |
| Patents Granted | 14 | 4 | 6 | 50% |
| Total Patents in Portfolio | 129 | 113 | 61 | -46% |
| New Licenses | 14 | 8 | 17 | 113% |
| Royalty Income | € 2.500.000 | € 440.000 | € 507.865 | 15% |
| Additional Added Value | NA | NA | € 3.135.770 | - |
| Spin-off companies | 7 | 2 | 2 | 0% |

Table 2:

*When an inventor contacts TTO to share his/her idea and this idea needs careful analysis, it is administered as an Invention (**Invention Disclosures**). If, after careful first analysis (both on novelty and on commercial applicability) it seems worthwhile to proceed and have the idea analyzed by V.O. (our partner patent attorney firm), then an Invention Disclosure Form is signed (**IDFs signed**). Following the analysis of V.O., a decision may be taken to file an application for patent protection (**Patent Applications**). This protection enables us to start negotiations with (commercial) partners on the valorization of such a protected invention.*

*When the governmental authorities have carefully evaluated the patent application and decided to grant the patent, we receive a confirmation (**Patents Granted**). This process may take considerable time. Therefore, there is no direct correlation between Patent Applications and Patents Granted.*

The active monitoring of our patent portfolio is an on-going task which ensures that we only invest in patents and patent applications that have commercial potential. The protection of inventions that have not been out-licensed, or patent applications that have entered into the national phase of the patenting process without having been licensed and/or have no strategic value to Erasmus MC, should be abandoned. This way we avoid the accumulation of a (too) large and expensive patent portfolio.

Total Patents shows the number of patent families (including patent applications) in our portfolio. We changed the way we count patents. This means that from 2015 onwards, we rather look at patent families instead of individual patents granted per country or jurisdiction.

The number of **New Licenses** being signed in 2014 was relatively low due to staffing issues. In 2015 a clear increase in the number of new licenses can be seen. This brings us back at the level of 2013. The **Royalty Income** dropped significantly in 2014 due to the fact that in 2013 the final payments for two license agreements with large royalty income were received and no more royalty payments will follow from those licenses (see also 'Financials'). In 2015, the royalty income was increased by ensuring accurate reporting from our Licensees and active follow-up on payments to be received.

A new KPI that was introduced is **Additional Added Value**. In some cases, TTO is able to provide advice and support on negotiations beyond the typical license agreements. When TTO has been successful in improving the conditions for a deal, it is counted as Additional Added Value. The Additional Added Value in 2015 is mostly linked to Clinical Trial and Material Transfer Agreements. TTO has created an Additional Added Value for several (mostly clinical) departments within Erasmus MC with a total gain of over €3 M. That being said, in some of these cases we only got involved in the very final stage of the negotiations. If TTO would be involved at an earlier stage, we would be able to better evaluate the opportunity and to even maximize the potential, when suitable and appropriate.

Spin-off companies are those companies that are established with the specific purpose of further developing Erasmus MC's IP (see also below for a detailed description).

One of the most prominent and visible ways in which we promote our professionalism is the creation of our "Wall of Fame". All the Non-Confidential Disclosures (NCDs)² that we create are presented on a wall at our department and whenever we out license one of the technologies, we clearly mark that NCD as 'SOLD'.

In addition, by renewing and regularly updating our LinkedIn page, we are able to reach a wide range of followers (over 170 followers year end 2015 from diverse industries and academia background) with an interest in the activities of TTO.

Next to the traditional activities the Business Development Team also offered new services:

- Clinical Trial Agreements: we became aware of the fact that clinicians often look at the budget of Clinical Trials from a 'cost approach'. We have a broader view and can therefore introduce a 'market approach' to the budget.
- Follow up on existing License agreements: literature shows that many Licensees (up to 95% of all license agreements) often under-report the royalties that they are obligated to pay. Close monitoring of the activities of the Licensee, discussions on the annual report and ensuring correct payments, have resulted in an increase in royalty income.

² An NCD is a one-pager that we use to promote Erasmus MC's inventions; f.i. at conferences, our website and on internet.

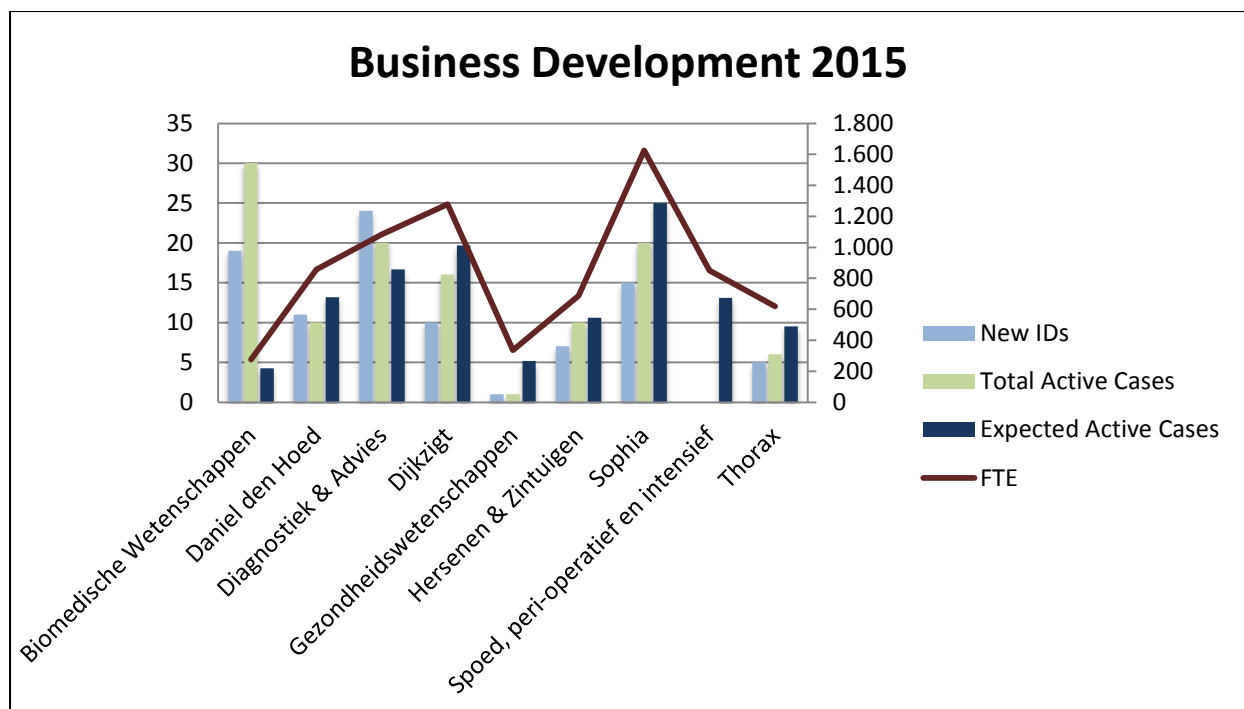
- Advice and support on negotiation strategies for agreements related to IP and services provided to external parties, other than contracts based on patents. This includes ensuring a fair compensation for consultancy provided to commercial entities and fair conditions when know-how is shared. Moreover, TTO Legal department is a competent and knowledgeable partner on trademark issues.

The added value of Business Development support is clearly demonstrated by the significantly increased number of IDs and IDFs that were shared with the Business Development team in the first 4 months of the year. Therefore, TTO was allowed to strengthen the Business Development Team with an additional FTE. The new Business Development Manager started her activities in November. By the end of 2015, the team consisted of 5,8 FTE, including one intern.

Figure 1: Business Development “Expected Active Cases” (dark blue bars, left axis) and “Total Active Cases” (light green bars, left axis) as distributed per Theme, related to the “relative size” of the Themes in FTEs (red line, right axis) in 2015.

“Total Active Cases” is based on the complete portfolio of active IDs that TTO is working on. By the end of 2015 these were 117 cases.

The light blue bars (left axis) indicate how the “New IDs” (96 in total) from 2015 were distributed over the different Themes.



To analyze how the work of TTO is distributed over the different Themes within Erasmus MC, Figure 1 shows how many activities TTO has initiated per Theme. It is clear that a Theme involved in a lot of fundamental research, such as “Biomedische Wetenschappen”, has close contacts to TTO, relative to the size of the Theme (in FTE). It is expected that this will continue to be the case, since fundamental research, in general, often needs the support from TTO to better understand the potential value of the outcome of the research to society (next to the scientific impact). We already had quite a large number of Active Cases for “Biomedische Wetenschappen” in our portfolio, in 2015 we received an impressive number of new IDs from them again.

It is interesting to look at another remarkable change that has occurred in 2015: the activities of TTO at Theme “Diagnostiek en Advies” has increased significantly. This may be a trend, although it is not very likely, as innovations are not something one can plan or predict.

Not all Business Development activities have an immediate monetary effect. Supporting negotiations on terms related to future commercialization of potential inventions in collaboration and consortium agreements is initially time consuming, but will ensure in the end that we are able to protect Erasmus MC’s knowledge from leaking away to industry without a fair compensation in the future.

17 new license agreements were signed in 2015, effectively doubling the number of licenses compared to 2014. These licenses included, amongst others: a mouse model, a survey (questionnaire), viral material for commercial research, technical solutions (imaging and hyperthermia), antibodies, data from studies and a mobile health application. Note that a number of these licenses are not based on patents, but on knowledge. The fact that TTO has been able to create awareness for IP in general (see footnote 1 on page 7), rather than patents only, this also increases the possibilities to out-license this knowledge more actively.

It is clear that by approaching scientists actively, and creating open lines of communication, TTO creates awareness for IP and the possibility to protect it. We are able to establish a productive collaboration, which results in defining the best opportunities and solutions to commercialize the outcome of the scientists’ research.

A few examples of exceptional cases in 2015 are provided below.

Clinical Trial Data

An Investigator Initiated clinical Trial was set up, executed and finalized, and the results were about to be shared with a commercial party that manufactured one of the various devices used in the clinical trial. The set-up of the agreement between the Erasmus MC team and the company was to combine the outcome of the clinical trial with the use of the company’s device. The draft agreement aimed to secure some funding to enable the Erasmus MC team to undertake further research and clinical trials in the same medical field. This draft agreement eventually reached TTO’s legal desk to be reviewed and approved. In cooperation with the Erasmus MC team, TTO re-initiated the negotiations aimed at getting a reasonable and fair value for the clinical trial results. Consequently,

TTO was successful in renegotiating the value of the deal and secured **fourfold** increase over the initially proposed amount offered for access to the results. By doing so, we won the trust of the company and we even secured substantial support in a follow up clinical trial by the same team.

Mouse models, repositories and MTAs

Animal and other biological models, such as cell lines, are necessary both in academic and industry research as a screening tool and therefore have (commercial) value in the development of new treatments and therapies. In 2015 TTO worked towards introducing a new set of tools that ensures the protection of ownership and commercialization of Erasmus MC animal models and their offspring. For this purpose, our animal facility has helped us to create awareness among our scientists on the necessity of signing a Material Transfer Agreement (MTA) beforehand when animals enter or exit the facility. This measure aims at securing the IP of the animal models, as well as the publication rights of our scientists.

In addition, TTO has signed a standing agreement with The Jackson Laboratory (TJL), a large American repository. There are currently 10 mouse strains from Erasmus MC deposited at TJL, coming from six different lead scientists out of four different departments. The agreement also establishes the terms and conditions for future deposits.

Finally, TTO has developed a good relationship with the EMMA platform to secure the rights of two mouse lines deposited there.

It should be clear that with professionalization of the technology transfer process, Erasmus MC will also more actively enforce its position and will fight against infringement, non-performance or shelving of its knowledge by Licensees.

We have been confronted with two infringement cases on Erasmus MC's IP, which we are handling at this moment.

TTO became involved in a legal proceeding to terminate a license agreement because of lack of activities by the Licensee. After terminating the license agreement, Erasmus MC was unfortunately called to court by the Licensee, however the judge ruled in favor of Erasmus MC. We regret that the Licensee felt the need to force both parties into a costly court case, whereas all the money and time spent in defending both our positions could have been invested better in further collaboration and valorization of the outcome of the research from Erasmus MC. However, non-performance or shelving of Erasmus MC's knowledge by a Licensee is not acceptable.

SPIN-OFF COMPANIES

Sensius

In Q2 2015, Erasmus MC and Sensius B.V. signed a license and collaboration agreement for the development and commercialization of the hypercollar. The hypercollar provides targeted hyperthermia to be used during radiation treatments, through which more effective treatments are created for patients suffering from head and neck tumors. The hypercollar was developed by the Department of Radiotherapy.

Sensius, a company specifically aimed at the development and commercialization of hyperthermia treatments, was founded by Thinkthrough and Lavoisier. This company and Erasmus MC TTO were in close contact for a lengthy period of time, before finally signing a license and collaboration agreement. Erasmus MC will provide Sensius with the expertise necessary to create a more solid foundation upon which the Hypercollar can be implemented. The inventors Prof. Dr. Gerard van Rhoon and Dr. Ir. Maarten Paulides will act as advisors on medical physics on behalf of Erasmus MC. Additionally, TTO has advised the Royal Dutch Cancer Foundation (KWF) and Sensius on the possibilities of a collaboration between the two parties.

**Slimmer Zwanger / Slimmer eten met je kind
(Smarter Pregnancy / Smarter eating with your child)**

An example of valorization of a non-patented technology is the “Slimmer Zwanger” concept of Prof. Dr. Régine Steegers-Theunissen from the Department of Obstetrics and Gynecology, and Pediatrics. The Slimmer Zwanger concept was already initiated in 2012 and aims to support couples that are trying to conceive. They can use Slimmer Zwanger to become aware of the positive influence of healthy eating and healthy life-style habits resulting in the increased chance to become pregnant (www.slimmerzwanger.nl).

In December 2015 a license agreement was signed with Slimmere Zorg B.V. The company was created around the concept of Slimmer Zwanger and aims at expanding the audience of the current application as well as building new applications based on the concept.

Slimmere Zorg B.V. is now responsible for all administrative tasks, which frees up the time of Prof. Steegers-Theunissen to focus on new initiatives.

PROOF OF CONCEPT Fund

The complete commercialization trajectory of advanced technologies, such as those developed in the Erasmus MC, is costly in both time and capital. Especially in the proof-of-concept phase, both time and capital often become scarce. Centralized funding (“eerste geldstroom”) does no longer suffice, but at the same time, the technology is not developed far enough for further financing via external (venture) capital. Additional developments of the technology are very costly and the time available for these further developments by scientific staff is often very limited as their primary task mostly centralizes around basic research.

This phase in technology development is often qualified as the “valley of death”. The limited funding opportunities often cause innovation projects to be discontinued, or early stage companies to run into bankruptcy. In a number of regions within the Netherlands, specific funds have been established to create financing possibilities for these early stage companies.

UNIIQ

In 2015, TTO started participation in the establishment of a specific Proof-of-Concept-Fund, called UNIIQ. UNIIQ will, from 2016 onwards, provide financing to such early stage initiatives. Aimed

specifically at investments in the life sciences & health sector, this fund will be active in an earlier stage than traditional venture capital or regional development funds.

UNIIQ is a collaboration between Erasmus MC, LUMC, TU Delft and Innovation Quarter. Each of the individual participants will have their own focus within the UNIIQ platform, but will join forces in the scouting, screening and evaluation of the applicants. Successful applicants can obtain from UNIIQ a maximum investment of €200.000, as well as access to the valuable network of all the partners involved in the fund.

UNIIQ will also apply for a contribution from the European Fund for Regional Development. In total, UNIIQ aims to acquire an investment capital of €22M.

The focus of Erasmus MC within UNIIQ is mainly on innovations within the Life Science & Health sector. By active participation under the flag of UNIIQ, Erasmus MC will have the opportunity to provide a much needed early stage capital facility for many of the companies founded by Erasmus MC, or those companies founded on the backbone of research from Erasmus MC.

TTO will play a central role in UNIIQ by providing a dedicated case manager as well as participating in the board of the fund itself. By facilitating an open and efficient collaboration between researchers, start-ups, TTO's business development managers and UNIIQ, TTO will further support the valorization process of Erasmus MC research.

LEGAL

It turns out that by actively opening our doors within the faculty building, and showing the added value of TTO to all Themes and departments, the number of contracts being offered for evaluation and approval increased drastically. After we saw the number of contracts handled by the Legal Team of the first 4 months of 2015, we already assumed that the result over the year 2015 would show a considerable increase as compared to the results of 2014. Therefore TTO was allowed to strengthen the team of Legal Counsels by 1,5 FTE. In November two new Legal Counsels started, which relieved some of the pressure on the team.

However, the increase of activities from the Business Development team's side also causes growth in the number of legal consultations related to those files. In conclusion, the pressure on the Legal Counsels continues to be high.

TTO's Legal Counsels evaluated and drafted (as the case may be) almost 1000 agreements in 2015, with 6,1 FTE (status ultimo 2015).

Table 3: Agreements reviewed

| | 2013 | 2014 | 2015 | Increase 2014 - 2015 |
|------------------------------------|------|------|------|-------------------------|
| Confidential Disclosure Agreements | 67 | 82 | 117 | 43% |
| Grant /Consortium Agreements | 105 | 106 | 122 | 15% |
| Consultancy Agreements | 40 | 46 | 68 | 48% |
| Collaboration Agreements | 47 | 36 | 52 | 44% |
| Clinical Trial Agreements | 93 | 132 | 184 | 39% |
| Material Transfer Agreements | 94 | 79 | 107 | 35% |
| Other Agreements* | 185 | 239 | 329 | 38% |
| | | | | |
| Total agreements reviewed | 631 | 720 | 979 | 36% |

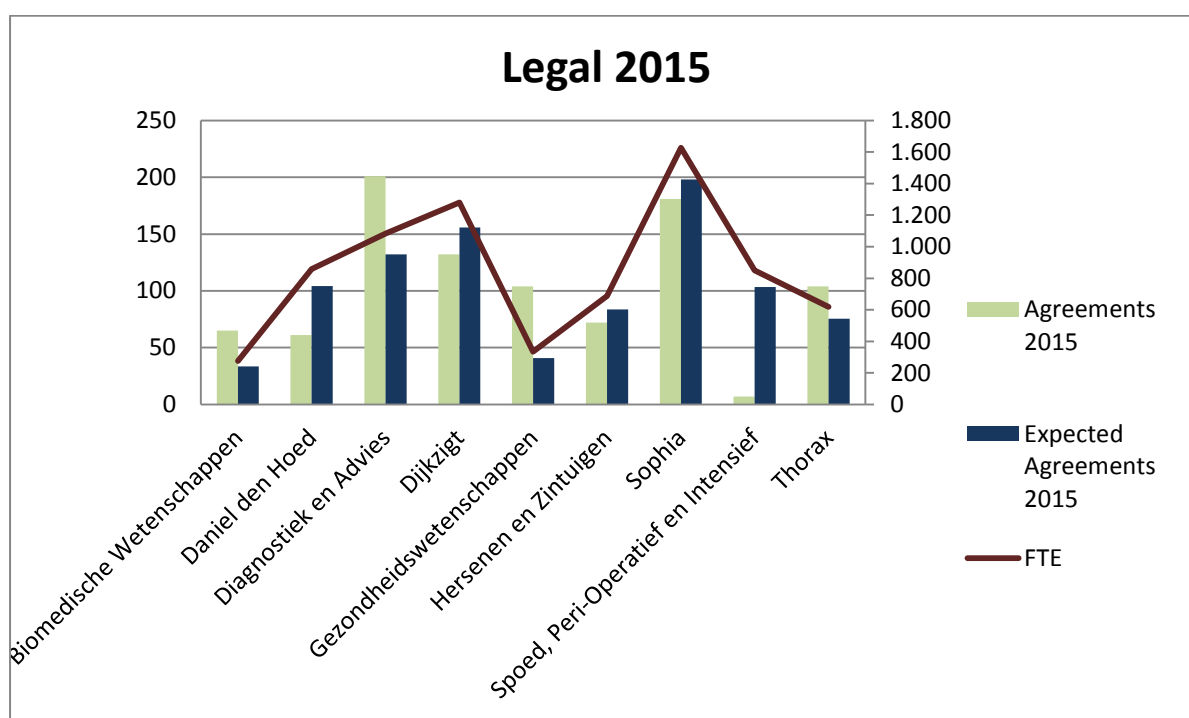
Table 3:

Our legal team handles an increasing number of contracts each year. However, the increase 2014-2015 (+36%) was significantly larger than the increase of 2013-2014 (+14%). An increase was expected, but the growth rate was much larger than could be anticipated. This sudden increase in agreements is most likely a result of a better positioned TTO.

: **Other Agreements consists of e.g. Lab-Service Agreements, License Agreements, Sponsor Agreements, etc.*

TTO has additionally been able to create a flexible workforce around the legal team to cover periods of longer response time to requests for support. The justification of this flexible workforce is linked to Horizon 2020 coordinator positions. The position of coordinator for such projects requires a lot of extra attention from our Legal Counsels due to the, often time-consuming, negotiations with a number of international collaborators. As a consequence other requests get delayed and result in increased response times.

Figure 2: “Expected Agreements” (dark blue bars, left axis) and “Agreements” (light green bars, left axis) as distributed per Theme, related to the “relative size” of the Themes in FTEs (red line, right axis).



Although the total number of contracts in 2015 differs significantly from 2014, the distribution of contracts over the Themes was similar.

An interesting observation can be seen when comparing the numbers from Legal (Figure 2) and Business Development (Figure 1) for “Gezondheidswetenschappen”: where Business Development has only limited activities in this Theme, for Legal the Theme produces many more agreements than would be expected based on the size of the Theme. A likely explanation for this difference is that “Gezondheidswetenschappen” is heavily involved in large (inter)national clinical studies that require proper contracting, but create only limited IP.

A few examples of cases handled in 2015 are provided below.

International collaborations including data originating from several parties

TTO was involved in a series of international collaborations and the formation of the legal structure thereof, among others Biomarker Development Center (Department of Neurology), Center for Personalized Cancer Treatment (Department of Medical Oncology), and EuroFlow Consortium (Department of Immunology). Research resulting in the creation of large, jointly developed (and owned) databases are seen more often. In some cases it is even useful to establish a separate legal entity for the handling of the joint interests of the parties involved.

These international collaborations include many different legal aspects. The first stage usually is the drafting of a proper collaboration agreement, which is the basis for the arrangements between all parties. When parties agree, it is possible to continue with the establishment of an entity (usually a foundation). When several parties contribute to the databases it is necessary to work out arrangements for the continuous use and the proper maintenance and handling of all data, so that the valuable databases remain available for further scientific research purposes.

Arrangements regarding the ownership of the results of the joint research have to be negotiated and included in all agreements. In an increasing number of cases arrangements in the collaboration agreements also point out the options for joint commercialization of results of such scientific research. These negotiations are often complicated and need careful processing by our Legal Team.

Copyright licenses

Upon the request of a research team, TTO advised on the license terms regarding the copyrights to a patient questionnaire for the evaluation of the progression of certain disease. In arranging the first license, TTO made sure that rights on translations were retained by Erasmus MC to secure the development of translations and therefore the accessibility to a broader patient population. Translations as such are insufficient for implementing these questionnaires. Validation studies (from the language and cultural standpoint) have to be conducted before such questionnaires can be used in different patient populations.

Currently, other companies conducting trials in the area for alternative medicines for the same disease are also interested in using the questionnaire in the course of their clinical trial program and have requested a license. While the financial impact may be relative (i.e. only minor royalties comes out of these specific licensing and collaboration arrangements), awareness and impact in the disease progression and treatment have a significant benefit from spreading this questionnaire to broader populations than just those for which it was originally developed and validated.

In conclusion, by proper protection of the IP by TTO the questionnaire represents a significant healthcare impact for patients affected by this disease.

Protection of academic freedom to publish

In collaborations with pharmaceutical companies, TTO focuses on, among others, the importance of Erasmus MC researcher's freedom to publish the results of these collaborations in scientific journals. Without an appropriate publication arrangement in the legal document, such freedom may be

compromised. Especially the publication of results from clinical research with human subjects, should never be jeopardized, as the international medical and scientific community may be deprived from important information regarding safety, efficacy and efficiency of medical treatments to patients. In each and every collaboration with industry, TTO will always protect the scientific freedom for Erasmus MC's researcher.

As already shown in Table 3, the increase in number of agreements being handled by TTO's Legal Department was very significant in 2015. We have reacted adequately by appointing two new Legal Counsels. However, the workflow remains a challenge and the response time to scientists who want to have their agreements evaluated is still longer than desired - despite a significant improvement. Currently, it is still unclear which percentage of the IP-related contracts of Erasmus MC scientists are seen by TTO's Legal Counsels. Will the numbers continue to grow at this speed, as, due to the increased awareness, more scientists are informed of the possibility of requesting the advice from TTO, or are we already reaching a saturation level? We follow the statistics in this sense very carefully, to find an optimum in the number of legal staff to the maximum number of agreements expected.

In the meantime, we also work on improving the user-friendliness of our web portal for uploading contracts to be reviewed to enable better management of the flow of requests.

Moreover, by investing more in the creation of combined business development/legal teams for certain complex files, Legal Counsels and Business Development Managers improve their joined skills and become more efficient in negotiating, drafting and reviewing agreements.

Also with respect to awareness activities, the involvement of the Legal Team has resulted in increased visibility and therefore easier accessibility of the team.

FINANCIALS

Historically, TTO has been responsible for acquiring a part of the budget necessary for its own operations. In 2015, Erasmus MC provided about 65% of the total TTO budget, while the other 35% had to come from additional services provided to both internal and external sources. For instance, by handling the administration of the WBSO subsidy, TTO received a service fee that provided for a stable part of the funding of the budget of TTO. A change in Dutch law has made it impossible for Erasmus MC to profit from WBSO from 2015 onwards, and therefore TTO is losing this service fee. Despite the loss of “WBSO Income for Erasmus MC”, TTO still managed to provide a significant added value to the Erasmus MC as a whole. The main reason for this was the introduction of “Additional Added Value” as a new Key Performance Indicator.

Table 4: Financials of TTO

| | 2013 | 2014 | 2015 | Increase 2014 - 2015 |
|---|--------------|--------------|-------------|-------------------------|
| Erasmus MC Contribution to TTO | € 710.365 | € 710.349 | € 756.132 | 6% |
| Licensing Income | € 2.500.000 | € 440.000 | € 507.865 | 15% |
| WBSO Income realized for Erasmus MC | € 664.762 | € 502.745 | ** | - |
| Other Income* | € 338.149 | € 295.968 | € 412.954 | 40% |
| Additional Added Value | not measured | not measured | € 3.135.770 | - |
| | | | | |
| Total added value for Erasmus MC | € 2.454.397 | € 232.396 | € 2.887.503 | *** |

Table 4:

Total added value for Erasmus MC is calculated as “Licensing Income” + “WBSO Income realized” + “Additional Added Value” - “Erasmus MC Contribution”.

“Additional Added Value” is the added value due to (re)negotiating of contracts or to better budgeting. By offering our economic and business techniques, TTO’s Business Development Managers are able to add value to already agreed budgets. The difference between the original budget and the new budget is calculated as “Additional Added Value”.

* **Other income:** consists of external contribution to our TTO, such as the WBSO service fee, EFRO-incubator management fees, VPR-funds, and incidental funding. This income is not considered as added value as TTO uses this directly in its operations.

** **WBSO Income realized:** for Erasmus MC in 2015 is not yet clear as described in “Introduction”.

*** A comparison of these numbers does not make sense as different elements contributed to the overall numbers over the years.

Note the increase in “Erasmus MC Contribution to TTO” in 2015 over 2014 was only 6%, while almost all other figures for Business Development and Legal increased with double digit percentages in 2015.

Following its Mission, new TTO strictly defined its core services but we also defined new services, that we feel should be included in our portfolio. After having participated in a number of trial projects in 2014, TTO has taken a more pro-active approach towards assisting scientists at an earlier stage of development. This support, despite not being included in the “traditional” services of TTO, has shown very promising results. In some cases, mostly for clinical trials, TTO became more involved in (re-)structuring, (re-)budgeting and (re-)negotiating deals with industry. As explained earlier, TTO is able to calculate the value of a collaboration from a ‘market approach’ while scientists frequently use the so-called ‘cost approach’. The value added to these contracts ranges from multiple thousands to sometimes even multiple millions of euros in total added value.

Despite not creating a formal trajectory for such services, the significance of the added value has encouraged TTO to continue providing these services in 2016. As the added value will mostly benefit the individual departments directly, TTO reports such value separately as “Additional Added Value”.

Only the tangible added value from TTO services is included in the calculations as shown in Table 4. However, TTO is also involved in creating added value for non-tangible IP rights, such as in kind improvements and retaining future IP-rights. This type of added value is not included in the calculation of the Additional Added Value, as it cannot be easily quantified.

Financials are important but the impact of the work of TTO is not only measurable in numbers. Societal impact and added value to patient care are at least as important as economic impact. These items are almost impossible to measure and to quantify.

ERASMUS MC INCUBATOR

The majority of the Erasmus MC Incubator's activities are related to supporting Erasmus MC's start-up companies by offering affordable lab- and office space in the Incubator, yearly advisory subsidies, and access to the knowledge and expertise of TTO and the rest of the Erasmus MC. While the EFRO-subsidy ended at the end of 2015, TTO is determined to continue its involvement in the Incubator, as does the Board of Erasmus MC, by ensuring the necessary funds to keep the Incubator active for another 5 years.

The Incubator currently houses three companies:

SkylineDx

2015 was an exciting year for SkylineDx, which continued to grow. The lead-product MMprofiler obtained the CE-IVD mark, which enables SkylineDx to commercialize the test in Europe. SkylineDx strengthened its management team with seasoned business executives with multi-decades of experience in the healthcare industry.

SkylineDx also incorporated an entity in the US and now has three employees there. The commercialization in the US will start once FDA clearance is obtained, which is expected in 2016.

Quorics

Quorics (formerly known as CardioGenx) went through more changes after two turbulent years (2013 and 2014). The company changed its name due to some pressure from a US competitor. Furthermore, the development of the lead product Angioprint (now called APprofiler) will continue under SkylineDx. The teams have been partially integrated. Quorics still has two European collaboration projects ongoing. It is expected that one of Quorics' therapeutic targets will be validated pre-clinically.

RiverD International

RiverD International started in 2012 and at the end of 2015 employed 11 FTEs. In 2014 RiverD introduced the 2nd generation *in vivo* skin analyzer: gen2-SCA.

New developments in the R&D pipeline are:

- Screening for Atopic Dermatitis (AD) risk
- Raman guided surgery to improve results in oncological surgery

ERASMUS MC HOLDING B.V.

Erasmus MC Holding B.V. is fully owned by Erasmus MC and manages Erasmus MC's participations in subsidiaries which are related to:

- knowledge valorization;
- care; and/or
- externally financed projects.

The goal of Erasmus MC Holding B.V. is to create and support the set-up of Erasmus MC subsidiaries. This support consists of management, financial advice, fiscal advice, consultancy and access to specialized facilities.

Erasmus MC Holding B.V. was founded on December 31st 2003 and ultimo 2015 holds, directly or indirectly, participations in 29 subsidiaries, of which 9 have minority participations (see Table 6).

Table 6: Overview of all participations of Erasmus MC Holding B.V. ultimo 2015.

| PARTICIPATIONS | % OWNERSHIP |
|-------------------------------------|--------------------|
| 2Move Implants B.V. | 5 |
| ABCDE-SIM B.V. | 41,9 |
| Agend B.V. | 100 |
| Arcarios B.V. | 1,31 |
| Cavadis B.V. | 1,52 |
| Eurza Arbo B.V. | 100 |
| Erasmus Biomedical Fund B.V. | 32,62 |
| Erasmus Pharma B.V. | 100 |
| Erasmus MC Ameland B.V. | 100 |
| Erasmus MC Diabetesstation B.V. | 78,4 |
| Erasmus MC Schiermonnikoog B.V. | 100 |
| Erasmus MC Vlieland B.V. | 100 |
| Harbour Antibodies B.V. | 35,17 |
| Erasmus Epidemiology Resources B.V. | 100 |
| HollandPTC B.V. | 33,33 |

| | |
|---|------------|
| Medical Oncology Research B.V. | 100 |
| MI&EUR B.V. | 100 |
| Nano4Therapy B.V. | 64 |
| Neurasmus B.V. | 100 |
| Quantib B.V. | 45 |
| Regionale Ontwikkelingsmaatschappij InnovationQuarter B.V. | 1,8 |
| Sophia Research B.V. | 100 |
| Thoraxcentrum Research B.V. | 100 |
| ViroNovative B.V. | 100 |
| Erasmus MC Zorg Holding | 100 |
| Apotheek A15 Holding B.V. | 50 |
| CBT Rijnmond B.V. | 50 |
| Geboortecentrum Sophia Holding B.V. | 50 |
| Poliklinische apotheek Erasmus MC B.V. | 100 |

The tasks of Erasmus MC Holding B.V. comprise:

- Stimulating and advising on entrepreneurship within Erasmus MC (for Erasmus MC spin-offs in collaboration with TTO). This service includes the possibilities of financial participation;
- Facilitate and support on the set up of businesses;
- Risk management for Erasmus MC and support for governance structures on large commercial projects and collaborations (non-spin-offs).

Erasmus MC Holding's primary focus during 2015 was on:

- improving the internal control processes;
- the Erasmus Holding structure and its governance;
- changes in the law of corporate income taxes and the impact on the participations of Erasmus MC Holding B.V.

In May 2015 the Director TTO was appointed as operational Director O&O - Erasmus MC Holding B.V. with responsibilities for Erasmus MC's participations in spin-offs out of Erasmus MC.

OUTLOOK 2016

General

Based on the successes of 2015, TTO will further develop and strengthen its positioning within Erasmus MC. We realize that we have not yet reached a 100% score when it comes to maximum awareness for TTO, and the support and tools that TTO can offer. Therefore, we will continue to create awareness via internal presentations and visits, and we will also continue to use other platforms to promote 'the knowledge creation process' among Erasmus MC personnel, such as our LinkedIn-page and intranet.

Furthermore,

- Awareness alone is not enough. TTO realizes more and more that students are the scientists and doctors of the future, and we need to focus our efforts on them as well. Although we are already included in some undergraduate courses, more initiatives need to be developed. With the newly installed EIT-Health programme by the European Commission, there are options to develop such initiatives.
- Support of international grant applications is a challenge as several departments within Erasmus MC are usually involved. With the establishment of the new structure of the Service Organization, a newly created group will take care of the central management of the support. TTO will continue to support this group, as requested.
- EIT-Health has announced the first calls. TTO will actively participate in creating a platform to further strengthen Erasmus MC's involvement in programs of EIT-Health.
- With the establishment of UNIIQ, Erasmus MC has a powerful tool that can be used to promote the creation of spin-offs and to overcome the first hurdles of creating a start-up.
- Our direct partnerships with the municipality of Rotterdam, the regional investment agency Innovation Quarter, Medical Delta and the two other TTOs within our vicinity (Luris, from LUMC/Leiden University, and TUDelft) will continue to be important, both by bilateral collaborations, as well as in larger consortia.
- We will keep in close contact with Erasmus Center of Entrepreneurship (ECE) and the recently started Cambridge Innovation Center (CIC), as these organizations may be instrumental in further strengthening entrepreneurship.
- Updates of several regulations will be implemented: 'Participation regulation', 'StAK', and 'Protection and Valorization of Erasmus MC Intellectual Property'.
- Erasmus MC adopted a pay-per-service system in 2015. TTO will not be exempt completely from this new system in 2016. Therefore, TTO is requested to define activities that can be seen as non-core and add-on services which could be invoiced separately to those departments that request these services. Options may be the support in writing business plans, trademark support, additional legal services, and additional financial support.

Business Development

- We will create Non-Confidential Disclosures (NCDs) for many more inventions, including older inventions which are already published but still have potential value.
- We will support (clinical) investigators to improve the business proposals/financial terms in Investigator Initiated Clinical Trials, but also for Industry Initiated Clinical Trials.
- We will pay increased attention to innovations in care and create more awareness for the need to protect these via the Valorization Programme Rotterdam (VPR).

Legal

- The importance of grants for Erasmus MC is obvious: it is however also clear that the pressure on TTO's Legal Team for the support in consortia agreements will increase. We will do our utmost to make sure that we will continue to have enough capacity for this support.
- Clinical Trials are an important source for external income. Therefore, not only the financial details are important but also the legal language of the agreement between parties. We will continue to provide assistance with such agreements (among other agreements).
- The Legal group will be more involved in the whole valorization process by strengthening the collaboration of Business Development and Legal in the negotiation process. As a new service, TTO will explore the possibility to register one of its Legal Counsels with the Dutch Bar Association, to become admitted to practice as an attorney-at-law. This way we will have the possibility to act faster and more cost effective on IP infringements and other (court-related) issues.

Erasmus MC Incubator

- The start of UNIIQ will create new possibilities to further strengthen the position of the Incubator in the Rotterdam Science Tower. When companies are supported by a loan from UNIIQ and need office and lab space, the Incubator is a logical location and fully equipped to further support the start-up.
- Alongside the partners within the Rotterdam Science Tower, we expect to organize several new events in the "... Meets Science" series.
- Together with Erasmus Center for Entrepreneurship (ECE) and the municipality of Rotterdam, we will further explore the options to strengthen the life science infrastructure in Rotterdam, especially around and in the Rotterdam Science Tower.

Erasmus MC Holding B.V.

- Erasmus MC Holding B.V. will be involved in the use of the new Proof-of-Concept Fund since the loans for the new start-ups will be paid from the Erasmus MC Holding B.V.
- With the new tax-ruling on profit-tax for all companies with limited liability (BVs), Erasmus MC Holding B.V. will need to look into the raison d'être of all participations carefully.

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