

# Technology Transfer Magic Sauce Ingredients - When and Where to Use Them

By

**Krishna (Balki)  
Balakrishnan, Ph.D., MBA**

Director  
krishna.balakrishnan@nih.gov

**Suryanarayana (Sury)  
Vepa, Ph.D, JD**

Deputy Director  
sury.vepa@nih.gov

**Rebecca Erwin-Cohen,  
Ph.D.**

Senior Technology Transfer Licensing  
and Patenting Manager  
rebecca.erwin-cohen@nih.gov

**Christopher Dillon, M.S., MBA**

Team lead  
christopher.dillon@nih.gov

**Ami Gadhia, JD, LL.M., CLP**

Senior Technology Transfer and  
Patenting Specialist  
ami.gadhia@nih.gov

NCATS' Office of Strategic  
Alliances (OSA)  
Rockville, MD.

## ABSTRACT

It is well known amongst the biomedical community that translating basic research findings into disease treatments or cures is a long and arduous journey, and one that requires the participation of a large number of individuals from a variety of backgrounds. Technology transfer, broadly defined as the sum of collaboration management, innovation management and intellectual property licensing, is central to the success of this translational process. This paper is a retrospective review of a select number of collaborations and case studies from the National Center for Advancing Translational Sciences (NCATS), a Center within the National Institutes of Health (NIH) that offers a fresh perspective on the field of technology transfer through the analogous lens of culinary arts.

Roughly 70% of all active projects within NCATS involve at least one outside collaborator, and nearly 60% of the patent portfolio at NCATS is managed by outside partners, thus providing us with a rich set of case studies to analyze and identify critical practices that we as a community must follow. The paper provides the context and the timing when these good technology transfer practice ingredients can be effectively employed. Just like the magic sauce ingredients that great chefs use are all well-known and commonly available, technology transfer professionals too have the tools listed in this paper freely available. However, these ingredients have to be used judiciously at the right time and in combination with other raw materials to get the desired results. The reader would appreciate that just as thoughtfully chosen magic sauce ingredients are required for talented chefs to produce delicious meals, great technology transfer efforts also require a judicious combination of strategies. Nothing less would be acceptable for all of us engaged in medical research.

## Introduction

This paper is a retrospective review of a select number of collaborations and case studies from the National Center for Advancing Translational Sciences (NCATS). It offers a fresh perspective on technology transfer activities through the analogous lens of culinary arts.

Practitioners of technology transfer understand that each licensing/collaboration agreement or relationship is unique and must be carefully nurtured. There is no "one size fits all" approach or a universal recipe for successful collaborations. A master chef too knows a similar reality. Chefs realize that each dish is unique and they need to judiciously employ the right ingredients at just the right time to prepare delectable dishes.

### Importance of Using the Right Ingredient at the Right Time

If we further explore the culinary analogy and apply it to technology transfer, we notice that the magic sauce ingredients that great chefs use are well known and commonly available. However, these ingredients don't necessarily taste delicious by themselves. But when they are used judiciously in combination with other ingredients and raw materials, they can produce mouthwatering dishes. Great chefs also know that each ingredient has a time and space. They know that, for example, ginger and soy sauce are central to Asian cooking but may ruin French or Italian dishes. Garlic, on the other hand, is equally welcome in American, Asian, and European cuisines. Great chefs also know that cooking encompasses both art and science just like the field of technology transfer, and this is where the culinary analogy of using the right ingredients at the right time really comes into focus for this audience.

As a brief background, all of the authors work at NCATS, which was established within the National Institutes of Health (NIH) in December 2011. NCATS' mission is to transform the translational process in biological research in order to bring more treatments for all people more quickly.<sup>1</sup> Soon after the inception of NCATS, its leaders recognized that such formidable goals can only be accomplished through broad collaboration amongst scientists on a global basis. Roughly 70% of all active projects within NCATS involve at least one outside collaborator, and nearly 60% of the patent portfolio at NCATS is managed by outside partners, thus demonstrating our commitment to extensive, public-private partnerships and collaboration. The Office of Strategic Alliances (OSA) plays an important role in these efforts by crafting optimum agreements with industry and academia to facilitate interaction and partnership with NCATS laboratories and outside scientists. Indeed, the "dishes" we prepare, i.e., the agreements that we craft, must satisfy a variety of palates and tastes.

This paper uses case studies and examples to show how the NCATS OSA team has judiciously used the various technology transfer "magic sauce" ingredients to overcome challenges and deliver results. Along the way, you will learn how some of these ingredients are central to the culture of teamwork and collaboration found at NCATS, and how these ingredients help the central translational science goal of NCATS, and are critical to the operation of tech transfer offices everywhere. The critical importance of teamwork for successful translation of ideas into tangible products is obvious to everyone. However, less clear are the challenges that come in the way of achieving win-win situations that in turn could catalyze further teamwork and lead to a virtuous cycle of success. Diversity of thought, inclusion of conflicting streams of experimentation, and the synthesis of a winning

pathway are all outcomes of well-structured team dynamics that result in successful collaborations.

## Overview of Ingredients

The word cloud in Figure 1 summarizes some of the various magic sauce ingredients. As earlier discussed, Translational Science is central to everything we do at NCATS. It is analogous to the principles of salt, fat, acid, and heat that are used almost universally in all cuisines. In addition to fresh ingredients, talented chefs play a critical role in producing delicious meals. At NCATS, we have a world class group of scientists who combine talent, education, and experience of the highest caliber. They collaborate with scientists from all over the world to generate extraordinary translational science platforms, enabling technologies, and tangible medical solutions. The lessons learned at NCATS can be applied to technology transfer operations throughout the world.

Not drawn to scale, these ingredients may be used alone or in combination with other ingredients. By themselves they may not be effective, but when used at the right time in the right way, they can help the central goal of translating basic science discoveries into useful health interventions.

### Customer Service and a Team Approach are Universal Ingredients

Let's start with a couple of the universal ingredients that we use in all collaborative agreements. We believe that success in technology transfer starts with great customer service. Before beginning any negotiation, the OSA staff engage in discussions and dialog to understand the customer needs and legal constraints. Such dialog creates a comfort zone for peers and customers alike and leads to a collaborative

FIGURE 1: Magic Sauce Ingredients



1 NCATS. <https://ncats.nih.gov/>

problem-solving mindset from the beginning. Earnest customer service pays great dividends throughout a relationship and helps to build deep relationships that last beyond the agreement itself.

The mindset of a team-based approach is another ingredient that can be used universally. A successful agreement requires collaboration from all parties. OSA staff initiate early and frequent contact with the collaborating scientists during all phases of the agreement negotiation and execution. We use those interactions to both learn from them about the science and to educate them about business and legal matters related to their collaborations. These negotiators attend some of the more critical scientific team meetings so that they can provide input whenever necessary. Further, a diverse team generates a broad variety of ideas and perspectives, making the outcome even stronger.

## Speed and Volume -- Two Sides of the Same Coin

The next two ingredients, speed and volume, are two sides of the same coin because they use common elements such as standardized agreements and processes. All agreement requests should be attended to promptly, yet there is a subset that get executed at a record speed. There are many examples of the benefits that this provides.

For example, and this may sound like an urban legend associated with the COVID times, but OSA negotiated and signed a Confidential Disclosure Agreement (CDA) during an introductory Zoom meeting between NCATS and a potential collaborator. Standardized, pre-negotiated templates have helped agreements in many operations move forward efficiently, such as two important NCATS programs, HEAL and ASPIRE.<sup>2,3</sup>

In terms of volume, we set a record with the National COVID Cohort Collaborative (N3C). Our plan engaged various stakeholders early in our agreement development process. The inclusion of these stakeholders produced a consensus template and within the span of just a few weeks, we executed hundreds of agreements. This paved the way for vast amounts of clinical data to be included into the N3C Enclave and for researchers to access these data for research projects. A remarkable challenge with the N3C agreements was to assemble as large a collaborative cohort as possible in as little time as possible in our urgent race to fight COVID. The N3C program has matured into the National Clinical Cohort Collaborative (N3C)<sup>4</sup> and continues to serve as an example of remarkable cooperation, flexibility, and the willingness for the data contributors and

users to conform to uniform template agreements. Another example of high-volume agreements to be executed materialized a few years ago within the Canvass Program.<sup>5</sup> To support this program, OSA developed a unique set of agreements that facilitated the acquisition of over 325 natural products and 50 assays. A high throughput screen was conducted to create a biological footprint of natural products. The data were then shared with the consortium after being anonymized, and eventually a summary of the findings was published.<sup>6</sup>

In general, when we establish CDAs for scientific programs such as the ones associated with the Therapeutic Development Branch, the Antiviral Pandemic Preparedness (APP), or HEAL supported projects, we encounter high volumes of agreements that need speedy execution. As a government agency, we must be fair, equitable, and transparent with our collaborators. Standardized agreements that are short and easy to read with reasonable terms help OSA meet these goals of NCATS.

## Innovation

One may wonder what role innovation plays in a staid, legalistic profession such as technology transfer. Examples of the benefits of bringing innovation and creativity to this process also abound.

Apart from generating often used creative solutions to solve negotiation roadblocks, the NCATS OSA has spent much effort in deeply understanding and analyzing the field of collaboration itself. Being part of NCATS, where innovation in all parts of the translational cycle is encouraged, we have spearheaded the creation of the Collaborative Research Collaboration Agreement (C-RCA). The C-RCA was born out of necessity but illustrates that innovation is a key ingredient for success in any technology transfer effort. The necessity for the C-RCA came from a situation in 2019, before which the standard practice at the NIH for dealing with joint inventions with academic institutions was quite straightforward. Prior to 2019, NIH collaborators taking the intellectual property (IP) lead could enjoy an exclusive license to joint IP without going through the process of the Notice of Intent to Grant an Exclusive License in the Federal Register (FR) for jointly developed IP.

In 2019, the legal policy picture changed. Going forward, FR notices would be required prior to granting any rights under an Inter-Institutional Agreement (IIA), unless the joint IP was a Collaborative Research and Development Agreements (CRADA) Subject

5 NCATS Canvass Program. <https://tripod.nih.gov/canvass/#>.

6 Kearney S.E. *et al.* 2018. "Canvass: A Crowd-Sourced Natural-Product Screening Library for Exploring Biological Space." *ACS Central Science*, 4(12) pp 1727 -1741 <https://pubs.acs.org/doi/10.1021/acscentsci.8b00747>.

2 NCATS HEAL. <https://ncats.nih.gov/heal>.

3 NCATS ASPIRE. <https://ncats.nih.gov/aspire>.

4 National COVID Cohort Consortium (N3C). <https://ncats.nih.gov/n3c>.

Invention and/or the jointly owned IP was developed under an NIH grant to the collaborator. In the case of collaborators who owned background IP and who sought to further develop and commercialize their technologies, the collaborator often took the lead in the IIA, without the undue burden of having to post FR notices. Requiring FR notices could delay IP management and stifle the transfer of the technology, while making collaborations with NIH less attractive. An ordinary research collaboration agreement (RCA) would not have the “teeth” of a cooperative research and development agreement (CRADA) and would not obviate the need for FR notices before granting an IIA. In collaboration with NIH colleagues, the NCATS OSA developed the C-RCA agreement mechanism that would address the need for a streamlined agreement with “teeth” and many of the CRADA benefits. While CRADAs and Research Collaboration Agreements (RCAs) are both collaborative agreements, they are dramatically different in terms of complexity, length, and transfer of funds. The C-RCA innovatively combined the best aspects of the RCA and CRADA to address the changing legal policy situation that we encountered in 2019. In the five years since becoming mainstreamed, the C-RCA has already been used in almost 40 collaborations, with NCATS accounting for over two-thirds of those agreements.

## Transparency

Transparency is an important value for building trust and cooperation among partners both external and internal. For external partners, repertoire has to be built in order to negotiate agreements effectively and there needs to be as much transparency as is possible.

Understandably, in a patent license agreement for example, the commercial entity taking a license (the licensee), may not show their P&L statement. However, they do need to draft a Commercial Development Plan for the technology and explain how they plan to deploy the technology. And while IP is listed in a license agreement, trust is not a section that is drafted therein and is inherent and yet foundational to the business transaction. Transparency and trust are equally as important for the internal scientists with whom the technology transfer/licensing professional works. For scientists who have dedicated their lives to addressing a small set of specific problems, their discovery or invention needs to be nurtured by the technology transfer professionals in a manner that conveys trust.

For example, OSA takes the internal scientists' viewpoints into consideration whenever possible without sacrificing objectivity and without violating any conflict-of-interest considerations. When we consult with scientists during license negotiations, we make sure to engage them in technical aspects such as the feasibility and appropriateness of the

commercial development plans, but we keep them away from financial terms to avoid any appearance of conflict of interest, real or perceived. In short, we provide responsible transparency.

## Cultural Sensitivity

When negotiating with international partners, it is imperative to show language and cultural sensitivities in addition to all other good negotiation etiquettes. A couple of quick examples illustrate this magic sauce ingredient. In one of NCATS' multi-party collaborative projects, NCATS OSA executed an agreement to repurpose a cancer drug, GM-CSF, for an ultra-rare pediatric lung disease. To advance the work, we needed access to Phase 1 safety data that the University of Tokyo (UT) was willing to share. The UT colleagues wanted to include the original scientist in all conversations, phone calls, e-mails, and other interactions, even though he wanted to excuse himself from the discussions. Several months later when the data sharing agreement was on the verge of being signed, there was a delay because one of the middle managers at UT, who was neither a signatory nor decision maker, was on vacation. UT felt that they needed this person's concurrence. The values of inclusivity and respect for order and hierarchy on the part of the UT counterparts needed to be respected here.

Each culture may have certain unique values that may seem trivial or non-consequential to an objective business mind, but they need to be respected if a deal is to be reached. Diplomats who frequently work in international waters know this only too well; as translational research takes on global range, cultural sensitivity becomes all the more important.

In another example, NCATS OSA was trying to negotiate a collaboration agreement with a Chilean university. The negotiation process had stalled many times due to language barriers. Fortunately, the Director of OSA at the time and the NCATS principal scientist involved in the collaboration were both fluently bilingual, and their Spanish skills came in very useful.

## Political Sensitivity

Political sensitivities are all the more challenging to navigate because of their sheer complexity and unpredictability. As an example, in the early days of the COVID pandemic, a published article pointed out the potential value of a Remdesivir metabolite, referred to as “compound 524.” There was speculation that compound 524 would be orally available and more effective at lower dosages and could be cheaper to manufacture than Remdesivir.

NCATS was asked to investigate the claims and possibilities. This was a politically sensitive case where NCATS needed to balance its commitment to public

transparency with the compound 524 manufacturer's corporate interests. Maintaining independence was of highest priority for the NCATS team. We had to navigate through several agreements so that we could get data and know-how from the original compound 524 manufacturer and patent holder in order to share those data with NCATS' subcontractors. In addition to these challenges, NCATS needed to comply with Federal Acquisition Requirements while maintaining good vendor relationships. These combined challenges were at times more complicated than solving the Rubik's Cube, where solving one relationship issue could potentially fray another one. The main motivator for all parties to reach consensus was their shared desire to meet the pandemic challenges and the needs of public health.

### Patience and Longevity -- the Other End of the Speed Spectrum

The list of ingredients that are useful in technology transfer is potentially endless but a good place to conclude would be the ingredients of patience and longevity, the very opposite of speed, the ingredient we started with. Collaborations in life sciences often have long lives because of the nature of the research and the risk of failure at all stages of the translational spectrum. Patience, trust, and relationship building are the characteristics that can provide the required longevity needed for successful translation.

The example given here relates to a rare bone disease called Fibrodysplasia ossificans progressiva (FOP), in which bones grow where they are not supposed to leading to the so-called "Ironman Syndrome." Scientists at the Massachusetts General Hospital (MGH) came to us with an early lead molecule that had several toxic liabilities. NCATS chemists, toxicologists, and drug metabolism scientists worked for several years to improve the molecule. To get to that point, both *in vitro* and *in vivo* assays and disease

models had to be developed for verifying the efficacy of the improved compounds. Eventually, NCATS and MGH jointly identified a good clinical candidate; MGH was able to spin out a startup company, Keros, that did initial clinical trials in Australia, as well as Phase 2 studies. Interestingly, Keros successfully went public in April 2020, during the first few weeks of the COVID pandemic. The remarkable point of this vignette is how the original collaborators stayed together throughout the project's ups and downs. The hope of an eventual cure for FOP is what kept all the collaborators bonded.

All of the examples presented above show that just as thoughtfully chosen magic sauce ingredients are required for talented chefs to produce delicious meals, great technology transfer efforts also require a judicious combination of strategies. At NCATS OSA, we use these principles to catalyze complex and successful collaborations that can produce results that cannot be achieved in isolation. We have noted clearly throughout this paper that all these ingredients are freely available to everyone. One needs only to choose the right ingredients consciously and deliberately at the right time to achieve superior results. Nothing less would be acceptable for all of us engaged in medical research.

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