BENEFIT-SHARING CASE STUDY

Yellowstone National Park and the Diversa Corporation

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OVERVIEW

MAIN ACTORS

Yellowstone National Park (YNP)

Yellowstone National Park is located in the United States of America in the southern portion of the northern Rocky Mountains, spanning the north-west corner of the state of Wyoming and the states of Montana on the north and Idaho to the west. The eastern boundaries mostly follow topographic divides, but the remaining boundaries are defined by compass lines (44°08'-45°07'N, 109°10'-111°10'W). Yellowstone National Park covers an area of 3,472 square miles (2.2 million acres or 898,714 hectares) and is surrounded by wilderness and wildlands in six national forests, the Grand Teton National Park to the south, and two national wildlife refuges. Taken together, these areas comprise the greater Yellowstone area, which is considered to be the Earth's largest intact ecosystem in the temperate climatic zone. Yellowstone National Park was established on 1 March, 1872, and is recognised as the world's first modern 'national park'. The area is designated as a United States Biosphere Reserve and World Heritage Site.

Yellowstone National Park is one of 375 U.S. national parks owned and managed by one of the U.S. federal land management agencies, the National Park Service, which, in turn, falls under the control of the US Department of the Interior. Yellowstone National Park management is responsible for managing scientific research activities in the park, regulating access to biological resources located within the park under Research Specimen Collection Permits, and negotiating more detailed access and benefit-sharing arrangements pursuant to Cooperative Research and Development Agreements.

Diversa Corporation

Diversa is a corporation that was organised in 1994 under the laws of the state of Delaware and now maintains its principal corporate headquarters in San Diego, California. The company was known as Recombinant Biocatalysis, Inc. (RBI) until the corporate name was changed to Diversa Corporation in August 1997. Diversa specialises in the discovery, modification, and manufacture of novel enzymes and bioactive compounds resulting from research on biological samples (including thermophilic microorganisms found in the thermal features of Yellowstone National Park). Diversa bases its research on molecular biology and functional genomics, and is particularly interested in sourcing materials from extreme environments. The company works in three principal areas:

(1) *Enzyme Biocatalysis* - exploration of biocatalytic functions and synthesis of pharmaceuticals and specialty chemicals enzymes;

(2) *Transgenic plants* - expression of enzymes and bioactive molecules in plants, for uses such as the insect and disease control; and

(3) *Discovery of recombinant natural products* - the discovery of bioactive products from recombinant sources for the generation of lead compounds for new pharmaceuticals. Rather than culturing organisms that express genes and compounds of special interest, Diversa captures nucleic acids by sampling DNA directly from the environment and cloning genes into

domesticated organisms. The company uses high throughput robotic screens to screen for enzymes and bioactive compounds from gene pathways.

Diversa is sourcing materials not only from the thermal features of Yellowstone National Park but also from other environments found in countries as diverse as Iceland, Costa Rica, and Indonesia. Since 1994, Diversa has discovered more than 600 enzymes and now serves customers worldwide.

World Foundation for Environment and Development (WFED)

WFED is an independent non-governmental organisation based in Washington DC that was established in 1992 to undertake creative problem-solving initiatives and to facilitate negotiations in the field of environment and development. In 1992, recognising the growing importance of balancing public-private partnerships to encourage the conservation and sustainable use of biological resources, WFED began to explore ways to facilitate negotiations on issues relating to access to and sustainable use of biological resources around the world. Since 1995, WFED has worked with Yellowstone National Park to clarify issues and facilitate negotiations relating to the development of a pilot programme at the park on conservation and a scientific research-focused bioprospecting programme. Through a Cooperative Agreement with Yellowstone National Park and in close cooperation with the National Park Foundation and the Yellowstone Park Foundation, WFED is coordinating development of the 'Yellowstone Thermophiles Conservation Project'.

OTHER ACTORS

The Edmonds Institute (EI) and the International Center for Technology Assessment (ICTA)

EI and ICTA are two NGOs that oppose the YNP/Diversa partnership. They petitioned the Secretary of the Interior to allow public review of the agreement before its signature. On 5 March 1998, joined by other NGOs, they filed a law suit against the U.S. Department of the Interior and the National Park Service for alleged violation of the Federal Technology Transfer Act of 1986, among other causes of action.

ECOSYSTEMS, SPECIES AND GENETIC RESOURCES

Yellowstone National Park's 3,472 square miles contain an estimated 60% of the world's terrestrial geothermal features and 80% of its geysers.[1] Cyanobacteria, eubacteria and archaea grow in the hot springs, geysers, fumaroles, and boiling mud pots of Yellowstone's geothermal ecosystem in temperatures from 40 to 93° Celsius.[2] The enzymes in these organisms, which continue to function in environments in which most living organisms would be destroyed, make them of interest to companies developing products that are made, or operate, in similar conditions.

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[1] Yellowstone Media Kit. http://www.biocat.com/index.html

[2] Lindstrom, Robert, 1997. Case study: *Thermus aquaticus*. Chapter 9 in Vogel, Joseph Henry (ed.) *From Traditional Knowledge to Bioprospecting*. Inter-American Development Bank, Consejo Nacional de Desarrollo del Ecuador.

TYPE OF BENEFIT-SHARING ARRANGEMENT AND EXPECTED RESULTS

Under a Cooperative Research and Development Agreement (CRADA) between YNP and Diversa, the company provided the Park with an up-front payment of US$100,000, payable in 5 yearly instalments of US$20,000, to be offset against any future royalty payments received by the Park under the agreement. The company has also transferred equipment such as DNA extraction kits and DNA 'primers' and has trained Park staff in some recent molecular biology techniques. In return, the company benefits from access to extremophilic microorganisms and other genetic resources in the Park, and from being permitted to use specimens collected earlier under Research Specimen Collection Permits for product development.

TIME FRAME ADDRESSED

The YNP/Diversa CRADA was signed on Sunday, 17 August 1997. The partnership is initially for five years, terminable upon 30 days' written notice by either party, although benefit-sharing, record-keeping and reporting obligations would survive the termination of the agreement. During the three years preceding the current agreement, Diversa had discussed the possibility of a CRADA with Yellowstone, while working under scientific research permits[3]. The partnership has been shaped by experience gained from a collection by another researcher in 1965. The 1965 collection led to the discovery of organisms that could grow above 72° Celsius, a temperature at which life was not formerly thought to exist, and the invention of a valuable commercial product (the Polymerase Chain Reaction, PCR). PCR became famous in the mid-1980s, but did not result in a share of benefits for the US Federal Government, or the US public. Based on this experience, in 1994-5, YNP decided for the first time that future research agreements should provide for the sharing of benefits in the event of commercialisation of a product derived from research on Yellowstone genetic resources. The Diversa partnership is seen as a 'model' for collaborations between the Park and commercial companies in the coming years.

RELEVANCE TO THE CONVENTION

Articles 7 ('Identification and Monitoring'), 8 ('*In-situ* Conservation'), 9 ('*Ex-situ* Conservation'), 10 ('Sustainable Use of Components of Biological Diversity'), 11 ('Incentive Measures'), 12 ('Research and Training'), 13 ('Public Education and Awareness'), 14 ('Impact Assessment and Minimising Adverse Impacts'), 15 ('Access to Genetic Resources'), 16 ('Access to and Transfer of Technology'), 17 ('Exchange of Information'), 18 ('Technical and Scientific Cooperation'), and 19 ('Handling of Biotechnology and Distribution of Its Benefits').

[3] Personal communication with Dr. Terrance Bruggeman, Diversa Corp, 17 February 1998.

CONTEXT

BIOLOGICAL RESOURCES

Microorganisms known as 'extremophiles' thrive in extreme conditions such as temperatures approaching 100 degrees or below 0 degrees Celsius, the high pressures found in the deep sea, or in extremely acid or alkaline environments. While the biological and chemical structures of most living organisms break down under such conditions, extremophiles thrive in them. The ability of the enzymes that are produced by extremophiles (dubbed 'extremozymes') to function in such conditions makes them of particular interest to research firms that participate in the development of pharmaceutical, agricultural and biotechnological products that operate in similar conditions.

An important category of extremophiles are referred to as 'thermophiles' ('heat-loving' organisms that thrive at high temperatures). Thermophilic microorganisms offer several major advantages for microbial technology, such as their ability to produce enzymes that are capable of catalysing biochemical reactions at far higher temperatures than the 'mesophilic' organisms that exist at normal temperatures. Thermophiles are more stable at conventional temperatures and able to operate in high concentrations of organic solvents.

Yellowstone National Park contains approximately 80 percent of the geysers and 60 percent of all terrestrial geothermal features found on Earth[4]. Prokaryotic, or single-celled, cyanobacteria, eubacteria and archaea grow in the hot springs, geysers, fumaroles, and boiling mud pots of Yellowstone's geothermal ecosystem in temperatures from 40 to 93° Celsius.[5] The diversity of the thermal environments in which these organisms live is compounded by great variations in chemical and mineral characteristics. NASA research at Yellowstone suggests that the Park's thermal environments offer some of the world's best preserved 'windows' on the origin of life on Earth as well as clues about the possibility of life elsewhere in the universe.[6] Access to the microbial biological diversity in Yellowstone is thus of considerable interest to the international scientific research community. While researchers estimate that less than one percent of the microorganisms living in the 10,000 thermal sites in Yellowstone National Park have been identified,[7] there is a growing inventory of newly described microorganisms first isolated at Yellowstone[8].

THERMOPHILIC MICROBIAL RESEARCH AT YELLOWSTONE

Fur trappers who visited the Yellowstone area in the early 19th century provided the earliest known written description of the brilliant colours characteristic of the microbial mats surrounding Grand Prismatic Spring in Yellowstone's Midway Geyser Basin:

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4 Yellowstone Media Kit.

5 Lindstrom, Robert, 1997. Case study: Thermus aquaticus. Chapter 9 in Vogel, Joseph Henry (ed.) *From Traditional Knowledge to Bioprospecting*. Inter-American Development Bank, Consejo Nacional de Desarrollo del Ecuador.

6 Personal communication, Preston Scott, WFED, 9 March 1998.

7 Yellowstone Media Kit.

8 See the Annexe to this paper.

> *At length we came to a boiling Lake about 300 ft. in diameter forming nearly a complete circle as we approached from the South side. The stream which arose from it was of three distinct colors from the west side for one third of the diameter it was white, in the middle it was pale red and the remaining third on the east side was light sky blue . . . . The water was of deep indigo boiling in an immense cauldron running over the white rock which had formed the edges to the height of 4 or 5 feet from the surface of the earth sloping gradually for 60 or 70 feet. What a field of speculation this presents for chemist and geologist.*[9]

Yellowstone National Park was established in 1872, partly because of the concentration of thermal features then described as 'natural curiosities'. Later 19th-century explorers of the area recognised that the colourful deposits surrounding many thermal areas suggested the presence of life[10].

In 1898, Captain James A. Erwin of the Fourth US Cavalry and the U.S. Geological Survey, the first acting Superintendent of YNP, issued the first Yellowstone collecting permit to W.A. Setchell of the University of California, who was researching thermophiles[11].

In the summer of 1966, Dr. Thomas Brock of Indiana University and one of his undergraduate students, Hudson Freeze, collected pink bacteria and mat samples from the outflow channel of Mushroom Spring at Yellowstone, at a temperature of about 69°C. By October 1966, Freeze had isolated a strain from this first collection, which he designated YT-1 (ATCC 25104). In 1969, Brock and Freeze published a paper based on Brock's taxonomic work and Freeze's study of its DNA, describing the organism which they named '*Thermus aquaticus*' (Taq).[12] Brock deposited representative cultures of Taq, as the organism is now commonly known, in the American Type Culture Collection (ATCC), in Washington D.C.[13]. The discovery of *T. aquaticus* was a scientific milestone, as it demonstrated that life could exist at far higher temperatures than had formerly been believed possible.

Kary Mullis, then a researcher at the American company Cetus Corporation, obtained a sample of YT-1 from the ATCC, for which the company paid US$35[14]. In 1984, he invented a procedure based on the enzymes from *Thermus aquaticus* for which he was to win the Nobel Prize for Chemistry a decade later[15]. Mullis purified an enzyme known as a thermostable DNA polymerase from Taq, termed Taq polymerase. DNA polymerases catalyse the synthesis of new DNA molecules, and if this reaction is conducted repeatedly, or 'cycled' it is possible to produce a considerable amount of DNA from what was originally a miniscule sample. This cycling of DNA

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9 Haines, A.L. (ed.), 1955. *Osborne Russell's Journal of a Trapper* (University of Nebraska Press), at page 99, quoting Osborne Russell who visited the Yellowstone area during the years 1834-1843, ca. 1840 at Grand Prismatic Spring in what later became Yellowstone National Park.

10 Weed, W. 1888, at pages 620-2. The geologist Walter Weed visited Yellowstone in 1888 as part of an expedition sponsored by the United States Geological Survey. He noted "there is reason to believe that the existence of algae of other colors, such as the red and yellow species common in Yellowstone springs, has generally been overlooked or the growth mistaken for mineral matter."

11 Lindstrom, Robert, 1997. Case study: Thermus aquaticus. Chapter 9 in Vogel, Joseph Henry (ed.) From Traditional Knowledge to Bioprospecting. InterAmerican Development Bank, Consejo Nacional de Desarrollo del Ecuador, and personal communication with Preston Scott, WFED, 9 March 1998.

12 Brock, T.D., and Freeze, H., '*Thermus aquaticus* gen. n. and sp. n., a non-sporulating extreme thermophile', in *J. Bacteriol.* 98: 289-297 (1969).

13 Brock, Thomas, 1995. Road to Yellowstone. Annual Review of Microbiology. The organism is catalogued as ATCC 25104.

14 Personal communication with Robert Lindstrom, 11 February 1998.

15 Wolf, Ron, 1994. Yellowstone Discovery: should US get profits? San Jose Mercury News. Monday 25 July 1994.

synthesis has been termed the 'Polymerase Chain Reaction' (PCR), and the technique is used in a wide range of applications, such as the DNA tests used in forensic medicine. During PCR, it is necessary to switch the reaction mixture repeatedly between low and high temperatures. When Mullis first invented the technique, he had been using an enzyme from a bacterium that operated at normal temperatures but that was inactivated during the hot periods of the cycle. When he replaced this enzyme with Taq polymerase, which continues to function during the hot periods of the cycle, this problem vanished.[16]

In 1991, the Swiss pharmaceutical company F. Hoffmann-LaRoche acquired from Cetus, all patent rights to PCR technology, for US$300 million.[17] Annual sales for the licensees of PCR equipment and supplies based on Taq are estimated to be approximately US$200 million, and growing, as the technique is applied to a wider range of biotechnology research, medical diagnostics, and environmental and forensic analyses.[18]

Other than the federal tax dollars paid by the companies in the U.S. who license PCR, which may arguably contribute to the US$20 million annual operating budget from the US Treasury to the Park Service to run Yellowstone National Park, the Park has not received a share of the financial benefits arising from the use of Taq and PCR. The absence of a direct share for the Park in the monetary benefits arising from the use of *Thermus aquaticus* can be largely attributed to two factors: the terms of the research permit issued to Brock by the Park Service in the 1960s, and the access rules of the American Type Culture Collection (ATCC) where Taq was deposited. The terms of Brock's research permit granted him permission to collect in Yellowstone but did not contain terms requiring him to share the benefits arising from research on the specimens collected.[19] When Mullis purchased a sample of Taq from the ATCC, he was not obliged to seek the permission of either the ATCC or of Yellowstone National Park prior to commercialising PCR, nor to share any of the benefits arising from this use of the enzyme.

This experience with Taq and PCR led the National Park Service to examine the options for benefit-sharing. Accordingly, in July 1996, Yellowstone was asked by the Director of the National Park Service to explore ways to position itself so as to maximise the benefits to resource conservation that could result from research on biological samples acquired from the Park.[20] The process that the Park followed is described below. The first partnership between a commercial company and a US National Park to result from this approach is that between Yellowstone National Park and the biotechnology company Diversa, the subject of this case study.

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16 Madigan, Michael T. and Barry L. Marrs, 1997. Extremophiles. Scientific American, April 1997.

17 Personal communication with Daniel Piller, Hoffman-LaRoche, 21 April 1998.

18 Lindstrom, Robert, 1997. Case study: Thermus aquaticus. Chapter 9 in Vogel, Joseph Henry (ed.) From Traditional Knowledge to Bioprospecting. InterAmerican Development Bank, Consejo Nacional de Desarrollo del Ecuador.

19 Wolf, Ron, 1994. Yellowstone Discovery: should US get profits? San Jose Mercury News. Monday 25 July 1994.

20 Personal communication with Preston Scott, WFED, 9 March 1998.

THE POLICY FRAMEWORK

Introduction

The United States signed the Convention in 1993, but has not yet ratified it. This means that the CBD is not recognised as law by the US courts, and its terms are not legally binding within the United States on US government agencies, private citizens or organisations.[21]

Under U.S. law, issues of ownership of and control over access to genetic resources are governed by a panoply of different legislative and regulatory regimes and common law, both at the federal and the state level. Ownership of genetic resources is often synonymous with ownership of the land on which those resources are found. In the United States, land may be owned by the federal government, the state governments**,** private individuals, including corporations, or groups of individuals.

Federal Lands

Almost one-third of the land surface of the United States is owned by the federal government[22]. The Federal government has primary management responsibility over these lands. The US Congress has the power within certain constraints to adopt legislation or create regulatory regimes concerning federally-owned territory, including regulations on access to these areas.

To administer its federal lands, the US Congress has established a series of federal administrative agencies, some located in different departments of the federal government. Each of these agencies is governed by a separate federal enabling act which sets out the terms under which the agency can manage the land under its control. In addition, many of these agencies have promulgated their own regulations to interpret and implement their management mandates.

Yellowstone National Park and the National Park Service

Yellowstone National Park is one of the 375 national parks owned and managed by one of the federal land management agencies, the National Park Service, which, in turn, falls under the control of the US Department of the Interior. The enabling act for the National Park Service, the National Parks Organic Act of 1916, and the regulations under the US Code of Federal Regulations (36 CFR 1, 'the Regulations'), set forth the parameters under which Yellowstone must operate.

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[21] Even if the U.S. had ratified the CBD and was thus a party, the CBD *per se* would not be enforceable in court, because it would not be considered self-executing. The position of the U.S. government is that existing legislation would be sufficient to implement the CBD should the U.S. become a party. Personal communication, Dr. Peter Thomas, U.S. Department of State, 30 March 1998.

[22] Plater, Zygmunt JB, Robert H. Abrams and William Goldfarb, 1992. *Environmental Law and Policy: A Coursebook on Nature, Law and Society*. West Publishing Company, St. Paul, Minnesota, U.S.A.
And: Environmental Law Institute, 1996: *Legal Mechanisms Concerning Access to and Compensation For the Use of Genetic Resources in the United States of America*, ELI, Washington, U.S.A.

Yellowstone Research Specimen Collection Permits

A system of permits to regulate access to and use of the Park's biological resources has been in place in Yellowstone National Park since the first permit was issued by Erwin to W. A. Setchell on Park Hotel stationary in 1898. Since 1983, the only collecting permits issued by Yellowstone have been permits for research on specimens within its territory according to the conditions for issuing specimen research permits set forth in Sections 1.6 ("Permits") and 2.5 ("Research specimens") of the Regulations.[23]

Section 1.6 grants to each superintendent of a national park the authority to issue the permits[24] allowed under various other sections of the Regulations, "consistent with applicable legislation, Federal regulations and administrative policies". Permits are based on a determination by the superintendent that "public health and safety, environmental or scenic values, natural or cultural resources, scientific research, implementation of management responsibilities, proper allocation and use of facilities, or the avoidance of conflict among visitor use activities will not be adversely impacted" by issuance of a permit.[25]

Section 2.5 of the Regulations establishes the terms under which Park superintendents may issue permits for collecting research specimens on Park land, an activity which is otherwise prohibited under the Regulations.[26] Section 2.5(b) requires that permits be issued only to "an official representative of a reputable scientific or educational institution or a State or Federal agency" for the purposes of scientific research or resource management. In addition, a research specimen permit may not be issued if removal of the specimen would have a detrimental impact on the Park's ecosystem.[27] The standard research specimen collection permit currently issued by Yellowstone incorporates the terms and conditions set forth in Section 2.5 of the Regulations.[28]

The scope of the genetic resources covered by the permitting system, however, remains unclear, and has yet to be determined by a court of law.[29] Section 2.5 (a) states that "[t]aking plants, fish, wildlife, rocks or minerals except in accordance with other regulations of this chapter or pursuant to the terms and conditions of a specimen collection permit, is prohibited"[30]. "Wildlife" is defined in Section 1.4 ("Definitions") as "any member of the animal kingdom [including] a part, product**,** egg or offspring thereof, or the dead body or part thereof, except fish".[31]

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[23] See 48 Fed. Reg. 30252 (June 30, 1983).

[24] A "permit" is defined under the Regulations as "a written authorisation to engage in uses or activities that are otherwise prohibited, restricted, or regulated." 36 CFR 1.4.

[25] 36 CFR 1.6. The NPS has decided that these determinations by Park superintendents are "adequate to ensure protection of park resources". 48 Fed. Reg. 30252, 30254 (June 30, 1983).

[26] 36 CFR 2.5 (a).

[27] Section 2.5(b) of the Regulations specifies that "[a] permit shall not be issued if removal of the specimen would result in damage to other natural or cultural resources, affect adversely environmental or scenic values, or if the specimen is readily available outside of the park area". Section 2.5(c) contains restrictions on issuing research specimen collection permits for threatened or endangered species. 36 CFR 2.5.

[28] Research authorization: Request to Perform Research in Yellowstone National Park. Permit Application. National Park Service, Yellowstone Center for Resources. PO Box 168, Yellowstone National Park, WY 82190, USA.

[29] Personal communication with Andrew Kimbrell, ICTA, 6 March 1998.

[30] 36 CFR 2.5(a).

[31] 36 CFR 1.4(a).

There has been no apparent clarification of the scope of the Regulations since 1994, when John Varley, Director of the Yellowstone Center for Resources, which manages the natural and cultural resources of Yellowstone National Park and issues collection permits, described the legal issues surrounding access to the genetic resources of US national parks as "immensely complicated". He continued his statement: "There are a variety of resources that are handled very differently . . .. You obviously can't come in here and take a moose or a grizzly and put it to some commercial application.... . That's clearly illegal." According to Mr. Varley, the application of the Regulations to microorganisms was unclear.[32]

While the exact scope of the genetic resources covered by permits may not be clear, Yellowstone and many other parks issue research specimen collection permits routinely. Historically, however, park research permits have not included provisions requiring permit holders to share with national parks the full range of benefits resulting from their research on collected material.[33] Furthermore, as the Research Specimen Collection Permits issued by Yellowstone restrict collectors to scientific or educational use of the material only, and prohibit use "for commercial profit, unless explicitly authorised by the superintendent [of the Park]", supplementary agreements with the Park are needed to cover research that may lead to commercialisation, and to stipulate benefit-sharing terms. The type of agreement which Yellowstone has decided to use in these circumstances is a Cooperative Research and Development Agreement[34] ("CRADA").

The Federal Technology Transfer Act and CRADAs

The Federal Technology Transfer Act of 1986 (15 USC 3710a *et seq.*) was enacted by the US Congress with the intention of encouraging cooperative research and technology transfer between the federal government and the private sector. A CRADA is a contract specifically authorised by this statute under which a private company contributes money and expertise to a "federal laboratory facility"[35] in order to augment its own research and in exchange for rights in any resulting useful or valuable discovery arising from the research. An implementing executive order[36] requires the heads of the various Federal agencies to delegate the authority to enter into CRADAs to designated "federal laboratories."

Under the Federal Technology Transfer Act, each Federal agency has broad discretion relating to laboratory determinations.[37] According to Preston Scott of WFED, the definition of the term

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[32] Wolf, Ron, 1994. Yellowstone Discovery: should US get profits? San Jose Mercury News. Monday 25 July 1994.

[33] Personal communication with Preston Scott, 9 March 1998.

[34] A CRADA is defined as "any agreement between one or more Federal laboratories and one or more non-Federal parties under which the Government, through its laboratories, provides personnel, services, facilities, equipment or other resources with or without reimbursement (but not funds to non-Federal parties) and the non-Federal parties provide funds, personnel, services, facilities, equipment, or other resources toward the conduct of specified research or development efforts which are consistent with the mission of the laboratory . . . ." 15 USC 3710a(d).

[35] The statute defines the term 'federal laboratory' to mean 'a facility or group of facilities owned, leased, or otherwise used by a Federal agency, a substantial purpose of which is the performance of research, development, or engineering by employees of the Federal Government.' 15 USC 3710a(d)(2)(A).

[36] Executive Order 12591.

[37] Section 15 USC 3710a(e) provides: "For purposes of this section, an agency shall make separate determinations of the mission or missions of each of its laboratories."

"federal laboratory" was intended to be broad in its scope.[38] He believes that national parks that host significant scientific research activities clearly satisfy this definition, and are thus qualified by law to enter into CRADAs under the statute.[39] In concurrence with this approach, the Department of the Interior, Yellowstone's parent Federal agency, has indicated its approval of Yellowstone's self-designation as a "federal laboratory facility" for
purposes of the Federal Technology Transfer Act of 1986.[40]

Commercialisation

Prior to 1995, all Yellowstone collecting permits stated that materials collected under those permits could not be commercialised.[41] Since 1995, however, the language of Yellowstone Research Specimen Collecting Permits has been changed to stipulate that "collections shall be used for scientific or educational purposes only, shall be dedicated to public benefit, and shall not be used for commercial profit, unless explicitly authorised by the superintendent [of the Park]".[42]

Under Section 2.1(c)(3) of Title 36 of the US Code of Federal Regulations, any "sale or commercial use of natural products" collected from national parks is prohibited. In entering into CRADAs with companies, according to Preston Scott of WFED, Yellowstone relies on a distinction between these prohibited activities and the discovery of useful applications of "research results" derived from work on collected specimens that could entail potential benefits for the park (whether these research results are commercialised or not)[43]. Thus, Mr. Scott maintains that while the collection and sale of a seedling from the Park would constitute a breach of Section 2.1 of the Regulations, the isolation of a gene from a microbial specimen sampled from the Park and its transformation into other microbial hosts from which a product is developed which is subsequently sold would not, because the genetic information used by the company is not a naturally occurring product.[44]

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[38] Mr. Scott cites in support a Senate Report that states, with respect to the term "federal laboratories", that '[t]his is a broad definition which is intended to include the widest possible range of research institutions operated by the Federal Government.' S.Rep. No. 283, 99th Cong., 2d Sess. (1986) at page 11." Personal communication with Preston Scott, 9 March 1998.

[39] Personal communication with Preston Scott, 9 March 1998.

[40] Personal communication with Preston Scott, 9 March 1998.

[41] Personal communication with Bob Lindstrom, Yellowstone Center for Resources, 9 February 1998. In the past, Yellowstone has issued permits to individual scientists, those based in academic institutions and those employed by companies. According to one source, several biotechnology companies obtained permits in this way, including Genencor International of Rochester, New York, Stategene Corp. of La Jolla, California, New England Biolabs of Beverley, Massachusetts and J-K Research Inc. in Bozeman, Montana, which "survives almost entirely by searching for novel microbes in Yellowstone and delivering samples to big biotech concerns." (Michael Milstein, Science, Vol.264, 29 April 1994.)

[42] Research Authorisation. Request to Perform Research in Yellowstone National Park. Permit Application. National Park Service. Yellowstone Center for Resources, PO Box 168, Yellowstone National Park, WY 82190. Provided by Bob Lindstrom, 11 February 1998.

[43] Drawing on this distinction, Preston Scott says that "[t]o date, no firm has asked Yellowstone for a permit to collect research specimens for the purpose of replication and subsequent commercialisation". Instead, from permitted research on specimens "potentially valuable information that may have useful applications in science and industry is derived, which may or may not ultimately have 'commercial' applications depending on the market and other variables." Personal communication, 9 March 1998.

[44] Personal communication with Preston Scott, WFED, 9 March 1998.

Relying on the same reasoning, the Diversa CRADA "does not permit or otherwise authorise commercial exploitation or other consumptive use of any biological resources obtained from the [Park]."[45]

Ownership of genetic resources in National Parks and Transfer to Third Parties

According to Title 36 of the Code of Federal Regulations, all specimens collected under research permits from US National Parks belong to the Parks.[46] Thus, under any agreement permitting research on specimens from Yellowstone National Park or the subsequent commercialisation of any products derived from them, the Federal government will retain ownership of those specimens. In the Yellowstone-Diversa CRADA, title over the specimens sampled in the Park and removed to Diversa's laboratories for research is not transferred to the company.[47] The specimens are still owned by the Federal government, but, as the CRADA does not deal with intellectual property rights, Diversa is free, under relevant US intellectual property law, to patent any innovations based on the specimens sampled, and to sell the resulting products.[48]

In accordance with Section 2.5 of the Regulations, the Yellowstone Permit Application provides that specimens collected and which have not been consumed as an authorised part of research must be accessioned and catalogued into Yellowstone National Park records and housed either at the Park Museum or with an agreed outside repository, under an Outgoing Loan Agreement.[49] According to Clause 6 of the Permit Application, "[t]he National Park Service reserves the right, in the interest of science, to designate the repository of all specimens removed from a national park or monument and to approve or restrict transfers of specimens between repositories".[50] Transfer by recipients of samples of genetic resources from Yellowstone to third parties is now subject to the approval of the National Park Service.[51]

Rules governing deposition of and access to samples in the American Type Culture Collection

The conditions of access to the American Type Culture Collection, where YT-1 was deposited in the 1960s, are another important aspect of the policy framework. The terms of access to specimens in the ATCC at that time contributed to the fact that the financial benefits that arose from the isolation of Taq polymerase, the invention of PCR and its subsequent application were not shared with Yellowstone.

In the 1960s, when Thomas Brock deposited YT-1 at the ATCC, the terms for the deposition and retrieval of specimens into and out of *ex situ* collections such as the ATCC were matters of far less

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45 Letter from the Superintendent, Yellowstone National Park to the Director, National Park Service dated August 22, 1997, ref. N30(YELL).

46 Text of standard letter from the Yellowstone Park Superintendent to Cooperating Researchers, Ref. N2621 (YELL).

47 Personal communication with Preston Scott, 9 March 1998.

48 Personal communication with Preston Scott, 9 March 1998.

49 Research Authorisation. Request to Perform Research in Yellowstone National Park. Permit Application. National Park Service. Yellowstone Center for Resources, PO Box 168, Yellowstone National Park, WY 82190. Provided by Bob Lindstrom, 11 February 1998.

50 Ibid.

51 Ibid.

policy and public interest than today. Microbial materials and their derivatives were generally exchanged freely in the scientific community or obtained from culture collections for a flat fee by non-commercial and commercial researchers alike.

Judging by this experience, the rules of access of the ATCC and other *ex situ* collections where genetic resources from Yellowstone National Park are deposited (whether pursuant to the obligations contained in the research permits or not) are likely to play a significant role in the Park's share of the benefits that arise from the use of its genetic resources. The provisions on continued ownership and the restrictions on transfer currently contained in Yellowstone's standard permit provide the Park with the right to monitor the transfer of materials collected under those permits.[52] However, it will be up to repository institutions to police compliance with restrictions on use and transfer, as well as to determine how to treat material from the Park which was deposited before those restrictions were put into place.

In 1997, the ATCC introduced a series of new generic material transfer agreements (MTAs) for investigators seeking access to materials within the American Type Culture Collection.[53]
In addition, all materials acquired by the ATCC from individuals and institutions such as Yellowstone National Park are now obtained under Material Acquisition Agreements stipulating who owns the deposited materials and how the ATCC and others can use them.[54]

Under this new regime, in order to access materials from the American Type Culture Collection, an individual or institution must first sign a material transfer agreement**.** The ATCC currently uses six different kinds of material transfer agreement, designed to meet the various circumstances and terms under which specimens are deposited in the Collection and supplied from it. All agreements expressly authorise use for solely non-commercial research by investigators requiring single or multiple access to the ATCC collections[55]. One agreement adds express restrictions on commercialisation and stipulates pre-publication notice and requirements for commercial licenses.[56] Another agreement allows for the exchange of specimens between ATCC and other institutions,[57] and a third sets forth conditions of use of materials on deposit at ATCC for patent purposes.[58]

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[52] Paragraph 6 of the permit reads "the National Park Service reserves the right...to approve or restrict transfers of specimens between repositories". Research Authorisation. Request to Perform Research in Yellowstone National Park. Permit Application. National Park Service. Yellowstone Center for Resources, PO Box 168, Yellowstone National Park, WY 82190. Provided by Bob Lindstrom, 11 February 1998.

[53] Personal communication with Dr. Leslie Platt, ATCC, 20 February 1998.

[54] Ibid.

[55] ATCC MMF2.2 and ATCC MMF2.4 respectively, available at http://www.atcc.org/mmf/mmf21.html.

[56] ATCC MMF2.2 available at http://www.atcc.org/mmf/mmf21.html.

[57] ATCC MMF2.5 available at http://www.atcc.org/mmf/mmf21.html.

[58] ATCC MMF2.6 available at http://www.atcc.org/mmf/mmf21.html.

The ATCC already contains materials isolated from Yellowstone, and the research permit system active at Yellowstone will inevitably lead to the deposition of samples in the ATCC. According to all the ATCC's material transfer agreements, any proposed commercial use of materials, replicates or derivatives must first be authorised by the ATCC as well as by any "Contributors" [59] that may retain a commercial interest. Upon notice of a potential recipient's interest in commercialising material from the ATCC, the ATCC or the "Contributor", as appropriate, will negotiate a commercial agreement with the recipient prior to shipping the requested material.[60]

PURPOSE / OBJECTIVES

Speaking of the potential of prospecting for extremophiles in Yellowstone National Park, Jay M. Short, the Executive Vice President and Chief Technology Officer of Diversa, commented that "[t]here is every reason to believe over the next five years we will identify microorganisms that may yield enzymes and bioactive molecules that will prove extremely useful for applications in medicine, biotechnology, food production, industrial chemistry."[61]

For its part, Yellowstone National Park wishes to promote scientific research, to raise revenue in order to support its conservation activities and to obtain a fair share of the financial and other benefits arising from research on Yellowstone genetic resources. Another objective is to minimise the tax burden on US citizens for the upkeep of the Park. If Yellowstone were not to require a share of the financial benefits from commercial prospecting for thermophiles, Yellowstone's resource management chief believes that such activities might be seen as "yet another giant rip-off of the people who have been paying their tax money to support this park".[62]

Yellowstone was asked in July 1996 by the Director of the National Park Service to develop a pilot programme to enable the Park to share in research-generated benefits for the first time. Specifically, Yellowstone was asked to develop a framework for negotiating benefit-sharing arrangements with the research community seeking access to Yellowstone's biological resources in a way that would strengthen the park's resource conservation activities; to develop a pilot bioprospecting programme that could be replicated as necessary by other national parks; and to do so in a way that would not discourage research activities in the parks under existing regulations.[63] The partnership with Diversa is the first agreement within this pilot bioprospecting programme.

While not motivated expressly by CBD-related considerations, Yellowstone National Park and Diversa believe that their agreement is consistent with all three objectives of the Convention, namely the conservation of biological diversity, the sustainable use of its components and the fair and equitable sharing of the benefits arising from access to genetic resources.[64]

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59 ATCC MMF2.5 available at http://www.atcc.org/mmf/mmf21.html.

60 Personal communication with Dr. Leslie Platt, ATCC, 20 February 1998.

61 Yellowstone Media Kit.

62 Milstein, Michael. Yellowstone Managers Stake a Claim on Hot-Springs Microbes. Science, Vol.270, 13 October 1995.

63 Personal communication with Preston Scott, WFED, 9 March 1998.

64 Ibid.

PROCESS FOR ESTABLISHING THE ARRANGEMENTS

The process used to establish the arrangements between Yellowstone National Park and Diversa involved two distinct aspects: the involvement of stakeholders in deciding Yellowstone policy on commercialisation of Yellowstone genetic resources and the role of different actors in the specific negotiations between Yellowstone National Park and Diversa.

The involvement of stakeholders in deciding Yellowstone policy on commercialisation

The CRADA system empowers government agencies to enter into research agreements with private companies that could result in the commercialisation of the results of the research. Although the Federal Technology Transfer Act has no explicit provision for public involvement,[65] the Superintendent of Yellowstone National Park consulted a number of stakeholders over the period from 1994 to 1995, when partnerships with companies conducting research on genetic resources obtained from the Park were under review. With some 250 research projects underway in the Park[66], the Park authorities are accustomed to working with the scientific research community. Over the issue of commercialisation, the Park held "The Old Faithful Symposium" in September 1995, at which the Park managers announced their intention to seek a share of commercial profits generated by products developed from extremophiles accessed in Yellowstone, and sought the response of the public and affected parties such as universities and biotechnology companies. The conference was attended by representatives of seventeen biotechnology companies, including Diversa, Promega, Eli Lilly and DuPont, members of the press, the National Biodiversity Institute from Costa Rica (INBio) and the World Foundation for Environment and Development (WFED).[67]

Park officials believe that common agreement emerged at the Old Faithful Symposium that the Park should enter into research agreements that would entitle users of genetic resources from the Park to commercialise products based on them, subject to adequate benefit-sharing commitments. However, no clear consensus emerged on the kind of benefit-sharing arrangements appropriate for the Park[68]. In order to consult an institution with considerable experience in this area, a delegation comprising members of the Park Service, WFED, Diversa and a journalist visited INBio to learn how that institution deals with scientific and commercial research of genetic resources within Costa Rica's national parks. INBio had several years' experience of access and benefit-sharing arrangements with companies, such as its well-known agreements with Merck & Co. of 1991 and 1994, as well as an agreement with Diversa.

John Varley, Director of the Yellowstone Center for Resources, estimates that since the Old Faithful Symposium, the Park has communicated its policy on partnerships with companies to the public at well over 100 venues, through meetings, television programmes and newspaper articles.[69]

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65 Personal communication, John Varley, Yellowstone Center for Resources, 18 February 1998.

66 Personal communication, Robert Lindstrom, Yellowstone Center for Resources, 9 February 1998.

67 Personal communication, Robert Lindstrom, Yellowstone Center for Resources, 9 February 1998, and Milstein, Michael. Yellowstone Managers Stake a Claim on Hot-Springs Microbes. Science, Vol.270, 13 October 1995.

68 Personal communication, Robert Lindstrom, Yellowstone Center for Resources, 11 February 1998

69 Personal communication, John Varley, Yellowstone Center for Resources, 19 February 1998

Participation in the negotiations between Yellowstone and Diversa

In May 1996, the Department of the Interior outlined its policy on CRADAs in a handbook entitled '*Technology Transfer: Marketing Our Products and Technologies (A Training Handbook for the US Department of the Interior)*'.[70] Yellowstone and WFED used this handbook as a "guide and standard" in preparing the agreement between the Yellowstone National Park and Diversa.[71] The basis of the agreement was first formulated by a staff member from Yellowstone National Park and a representative from the company. Once a first draft was prepared, the agreement was passed up through the Park's line management to the Superintendent. At this stage it was refined, then passed to the Secretary of the Interior for approval.

The Park used the World Foundation for Environment and Development to assist in negotiating the CRADA with Diversa. WFED's director, Preston Scott, has had wide experience with licensing arrangements. WFED worked *pro bono* for the Park for two years, and was subsequently retained by the Park as a consultant. Furthermore, the National Park Service was able to consult other organs of the U.S. government involved in CRADAs and access and benefit-sharing. The National Institutes of Health were consulted to confirm that the royalty ranges agreed in the CRADA with Diversa were fair, when compared with experience in other partnerships with companies.[72]

Subsequently, some organisations have registered their opposition to the agreement. The Edmonds Institute, a non-governmental organisation, did not contact the Park directly to discuss the proposed CRADA and the partnership with Diversa,[73] but, on 1 July 1997, it filed Freedom of Information Act requests with the Office of the Secretary of the Interior and with the National Park Service, hoping to see the terms of the CRADA. According to Park staff, it would have been difficult to open the agreement to public review during negotiations, as the terms of the CRADA upon which the public might wish to comment would not have been developed yet.[74]

On 15 August 1997, the Edmonds Institute and the International Center for Technology Assessment filed a petition with the Secretary of the Interior and with the National Park Service, requesting that the proposed CRADA be dropped, and that information concerning the agreement be released.

The CRADA between Diversa and Yellowstone was signed on Sunday 17 August 1997, during a visit to Yellowstone's 125th anniversary celebrations by Vice President Al Gore, Interior Secretary Bruce Babbitt and National Park Superintendent Robert Stanton.[75]

Under the terms of the Federal Technology Transfer Act, each CRADA negotiated and signed between a Federal laboratory and a company is subject to a statutory 30-day review of its terms by the head of the relevant Federal agency.[76] Since the Yellowstone-Diversa agreement is the first of its kind, Diversa volunteered an additional 60-day period before finalisation of the agreement.

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70 Personal communication from Preston Scott, 9 March 1998.

71 Letter from the Superintendent, Yellowstone National Park to the Director, National Park Service dated August 22, 1997, ref. N30(YELL).

72 Personal communication, Dr. Carolyn Ericson, 22 April 1998.

73 Personal communication, John Varley, Yellowstone Center for Resources, 19 February 1998.

74 Personal communication, Bob Lindstrom, Yellowstone Center for Resources, 11 February 1998

75 Marshall, Eliot (ed.) Sciencescope, www.sciencemag.org Science, Vol. 277, 22 August 1997; Yellowstone Net News Page, 1997 News Stories: August 19.

76 15 USC 3710 a (c) (5).

During this period, the Park held public comment meetings at the National Park Service and the Department of the Interior, and the Clinton White House reviewed the agreement.[77] The company has now transferred technology to Park personnel, made the first payment to the Park in August 1997 and established the scientific programme of work with the Park. The 'grace' period lapsed in November 1997.

However, the NGOs' opposition to the partnership continues, as they believe the CRADA involves "selling off public resources".[78] According to Beth Burrows of the Edmonds Institute, "[t]hese are business deals they're making, and the product is something that belongs to the people of this nation".[79]

On 21 January 1998, the National Park Service Director Robert Stanton denied the petition to drop the agreement between Yellowstone National Park and the Diversa Corporation, but on 6 February 1998, the Department of Interior settled the Freedom of Information Act lawsuit out of court, paying the Edmonds Institute approximately US$8,000 in legal fees, and making most of the requested information available to the NGO.[80] However, the Department did not provide the Edmonds Institute with a copy of Appendix B of the CRADA between Yellowstone and Diversa, which sets out the financial details of the agreement.

According to Preston Scott of WFED, this is because US law protects "trade secrets and commercial or financial information obtained from a person [that is] privileged or confidential" from unauthorised disclosure pursuant to Exemption 4 under the Freedom of Information Act.[81] The royalty rates and related payment information contained in the Yellowstone-Diversa CRADA relate specifically to Diversa's commercial and pricing interests in products that may be derived from research results involving biological samples acquired from Yellowstone National Park. The rates are the result of CRADA negotiations involving confidential business proprietary information obtained from Diversa, and Diversa has advised Yellowstone that disclosure of the information would be harmful to the company's commercial interests inasmuch as it relates to cost issues relevant to the company's pricing policies.[82] Confidential information obtained by the Government pursuant to a cooperative research and development agreement is also protected from unauthorised disclosure pursuant to the Federal Technology Transfer Act of 1986.[83]

Mr. Scott explains that disclosure of confidential information could undermine the ability of Yellowstone to negotiate beneficial financial arrangements (which include but are not limited to

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77 Personal communication with Terrance Bruggeman, Diversa Corp, 17 February 1998.

78 Edmonds Institute Press Release, 3 December 1997.

79 Ibid.

80 Edmonds Institute Press Release, 5 March 1998. The docket number of the papers filed with the court on 23 September 1997 is 97-CV-2190.

81 Personal communication with Preston Scott, 9 March 1998.

82 A distinction may also be drawn between monopolistic and competitive situations. In monopolistic situations such as a concession to run a food stand in a park, it can be argued that transparency and accountability requires full disclosure of financial information. In the case of non-exclusive arrangements such as the Yellowstone/Diversa CRADA, however, some would argue that it is reasonable to keep financial terms confidential to encourage competition and investment. Personal communication with Dr. Peter Thomas, US Department of State, 30 March 1998.

83 Personal communication from Preston Scott, 9 March 1998.

royalty rates) with other firms in the future, because firms will not engage in negotiations without the assurance that confidential information will be protected.[84]

On 25 February 1998, the Edmonds Institute filed a further Freedom of Information Act lawsuit against the National Park Service for withholding from public disclosure the financial arrangements of the Yellowstone-Diversa CRADA in the withheld Appendix B[85]. Shortly thereafter, on 5 March 1998, the Edmonds Institute, the International Center for Technology Assessment, the Alliance for the Wild Rockies and another Plaintiff, Phil Knight, filed a complaint against the Department of the Interior and the National Park Service to cease implementation of the Yellowstone-Diversa CRADA[86].

The NGOs' complaint is based on three major allegations.[87] First, it alleges that the Yellowstone-Diversa CRADA violates the Federal Technology Transfer Act, since that statute only allows federal laboratories to enter into CRADAs with private entities to exchange laboratory related resources, whereas the CRADA in question is between a national park and private entity, and concerns the extraction and exchange of natural resources.[88]

Second, the NGOs allege that the CRADA violates the intent and implementation of the National Park Service Organic Act of 1916[89] and the Yellowstone National Park Organic Act,[90] both of which require the Park to leave the Park environment unspoiled and prohibit the sale or commercial use of natural products from the national parks, on the basis that the CRADA provides for extraction and commercialisation of genetic resources from Yellowstone.

Finally, the NGOs claim that the CRADA has not been subjected to the public scrutiny to analyse its environmental or socio-economic impacts required under section 102(2)(c) of the National Environmental Policy Act (NEPA).[91]

Discussions within different departments of the U.S. government during 1998 led to the amendment of the CRADA between Yellowstone National Park and Diversa in April.[92] The period of review, required by statute to last 30 days, and originally extended voluntarily by Diversa to 90 days, was extended for an even longer period, while different government officials reviewed the original agreement for compliance with the relevant regulations and consistency with government policies, and discussed proposed changes with the company.[93] The new CRADA is substantially the same as the original agreement, but reflects two main changes: one set of changes concerns the terms of

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84 Ibid.

85 Edmonds Institute Press Release, 5 March 1998. The docket number of the papers filed with the court on 25 February 1998 is 98-CV-482.

86 Edmonds Institute Press Release, 5 March 1998.

87 Edmonds Institute Press Release, 5 March 1998, and personal communication with Andrew Kimbrell, ICTA, 6 March 1998.

88 They also claim that the CRADA violates section 3710a(f) of the statute, which provides that CRADAs cannot limit or diminish the existing statutory authority of any Federal agency. Edmonds Institute Press Release, 5 March 1998, personal communication with Andrew Kimbrell, ICTA, 6 March 1998 and Complaint submitted by the Edmunds Institute et al. to the US District Court for the District of Columbia on 5 March 1998.

89 16 U.S.C. §1.

90 16 U.S.C. §21.

91 42 U.S.C. §4332(2)(c).

92 Personal communication, Dr. Eric Mathur and Dr. Carolyn Ericson, Diversa, 22 April 1998.

93 Ibid.

the benefit-sharing arrangement, and the other concerns some minor changes of the language. No other substantive changes were made, and the scope of the agreement and the definition of terms remain the same.[94]

In the amended CRADA, the value of the non-monetary benefits is raised from the original commitment of US$75,000 during the five-year duration of the CRADA, to a commitment of this sum each year.[95] While the royalties still range up to 10% for different categories of product, a new clause modifies them by raising them in the event that a product achieves high sales in the bracket US$50m to US$200m.[96]

CONTENT AND IMPLEMENTATION OF THE ARRANGEMENTS

INPUTS

Yellowstone National Park

The primary contribution of Yellowstone National Park to the agreement with Diversa is to grant the company access to the Park and to samples of genetic resources within it, and to protect the Park's ecosystems and genetic resources so that genetic resources continue to be available for research. However, the expertise of Park scientists and data held within the Park Resources Center also enable Yellowstone to bring other skills to the partnership. The detailed knowledge of Park staff on Yellowstone's thermal features can assist researchers by directing their work in particular environments, for example by identifying thermal features with a certain temperature or pH. Since some of the thermal features offer a dangerous environment for people, Park staff also work closely with researchers, guiding them through the Park's habitat for their own safety and to protect the environment.

Diversa Corporation

The role of Diversa Corporation is to collect samples in collaboration with Park officials and to conduct research and development upon them.

Diversa Corporation bases its research on molecular biology and functional genomics, and is particularly interested in sourcing materials from extreme environments. Diversa is sourcing materials not only from the thermal features of Yellowstone National Park but from hydrothermal vents and volcanoes in locations as diverse as Antarctica, Iceland, Costa Rica and Indonesia. According to Diversa's Chief Executive Officer, Dr. Terrance Bruggeman, the company is committed to ensuring that all of its agreements for access to genetic resources comply with the CBD and related national laws. The company works in three areas: the discovery of enzymes to replace chemical catalysts in various chemical products and processes; the expression of proteins in

[94] Ibid.
[95] Ibid.
[96] Ibid.

plants, for uses such as the manufacture of bioinsecticides; and the discovery of bioactive products from recombinant sources for new pharmaceuticals.

Some of Diversa's scientific staff have worked in Yellowstone for 6 years, although the company itself was formed four years ago, and has been working in Yellowstone ever since. Until August 1997, Diversa worked under the Yellowstone Research Specimen Collection Permits described above, which restrict the collector to scientific or educational use of the material only, and prohibit use "for commercial profit, unless explicitly authorised by the superintendent [of the Park]". The new CRADA is the first agreement in which the superintendent authorises the company to commercialise products derived from the genetic resources sampled from Yellowstone, including those collected in earlier years under Research Specimen Collection Permits.

In its work on recombinant natural products, Diversa isolates DNA directly from raw samples of microbes and introduces it into established laboratory organisms, rather than isolating and culturing the microbes that express genes and produce compounds of special interest. The company uses ultra high throughput robotic screens to identify enzymes and bioactive compounds. In the company's laboratories, research scientists isolate DNA from the microbes present within the raw samples acquired from Yellowstone National Park. The DNA is then introduced into microbial hosts to generate a 'gene library'. These microbial hosts are typically bacteria that can be easily grown in the laboratory. Gene libraries generally contain the majority of DNA isolated from raw samples of microbes and this DNA can then be screened for the expression of specific enzymes. For example, researchers looking for an enzyme to degrade cellulose would feed cellulose to bacteria containing genes from the library. If any specimen showed an increased ability to degrade cellulose, the researchers would know that they had identified a functional gene producing an enzyme of interest.

Diversa is already developing enzymes sourced from Yellowstone microbes, for pulp bleaching in paper making and for "stone washing" blue jeans.

BENEFITS

The Yellowstone-Diversa partnership entails the sharing of benefits of both a monetary and non-monetary kind.

Monetary benefits to Yellowstone National Park

Diversa provided Yellowstone National Park with an up-front payment of US$100,000, payable in 5 yearly instalments of US$20,000, to be offset against any future royalty payments received by the Park under the agreement. The CRADA also contains provisions for the payment to Yellowstone of royalties in the event that a product derived from Yellowstone genetic resources yields a profit.

Under the law governing CRADAs, Yellowstone is authorised to 'accept, retain and use' the up-front annual funds contributed by Diversa[97], whereas any subsequent royalty payments eventually received by Yellowstone from Diversa must be shared between Yellowstone and the National Park

[97] 15 USC 3710a(b)(1).

Service[98], so that some of Yellowstone's financial benefits from the arrangement will be shared with its sister Parks.

Monetary benefits to the World Foundation for Environment and Development

For its services to Yellowstone National Park in supporting negotiations with Diversa, WFED has, thus far, been paid US$28,000.[99] WFED continues to act as consultant to the Park.

Non-monetary benefits to Yellowstone National Park

The partnership also involves a component of donation of equipment to the Park, and training of its staff. In the original CRADA, this was valued at US$75,000 throughout the lifetime of the agreement, but in the amended agreement, the value of 'in-kind' benefits has been raised to US$75,000 in each of the five years of the agreement. Diversa has given Park staff equipment such as DNA extraction kits and the DNA 'primers' needed to start the Polymerase Chain Reaction to detect target DNA. Scientists from Diversa and Yellowstone work together about once every two months. Park staff have visited the company's laboratories, and Diversa scientists have helped train Park staff in the latest molecular biology techniques for a number of Park projects. One example is the transfer of biofilm technology and training in its use, enabling Park staff to conduct a visual identification of *Thermus aquaticus*. Diversa scientists have trained Park staff in DNA fingerprinting techniques, and have helped the Park with projects quite unconnected to the company's own research activities, such as the detection of Brucellosis in Yellowstone bison using PCR process technology.[100] The annual benefit of this technology transfer is valued at US$75,000 per year.[101]

Monetary benefits to Diversa Corporation

If any product succeeds through the company's discovery and development programmes, the Diversa Corporation will obtain, as monetary benefits arising from its partnership with Yellowstone, any net profits on sales of the product concerned.

98 15 USC 3710c(a)(1)(B).

99 Personal communication with John Varley, Yellowstone Center for Resources, 19 February 1998.

100 Personal communication, Bob Lindstrom, Yellowstone Center for Resources, 11 February 1998.

101 Personal communication, Terrance Bruggeman, Diversa, 17 March 1998.

Non-monetary benefits to Diversa Corporation

Diversa Corporation receives non-exclusive access to the genetic resources in the unique habitats of Yellowstone National Park, including not only microorganisms in the thermal features, but genetic resources in other Yellowstone ecosystems, such as the alpine tundra. The company also benefits from the expertise of Yellowstone scientists in conservation and the sampling of materials, and information maintained on the Yellowstone database on the various ecosystems within the Park. A further benefit that Diversa derives from the CRADA with Yellowstone is permission to commercialise products derived from the genetic resources obtained from Yellowstone under the Research Specimen Collection Permits under which the company worked in the Park for the three years prior to negotiation of the CRADA.

SUMMARY OF INPUTS AND BENEFITS IN THE YELLOWSTONE NATIONAL PARK AND DIVERSA PARTNERSHIP

	YELLOWSTONE NATIONAL PARK	DIVERSA CORPORATION	WFED
INPUTS	• Conserves the biodiversity in Yellowstone National Park • Entered into CRADA with Diversa granting access to the genetic resources of the Park • Park staff accompany Diversa staff to take samples • Park staff contribute knowledge about the Park's thermal features and methods of collecting that minimise environmental damage	• Samples microbes from the Park environment, isolates DNA and clones genes into laboratory microbes to screen them for interesting activity • Will pay YNP $100,000 in 5 yearly instalments of US$20,000 and undisclosed royalties in the event of commercialisation • Training and equipment for YNP staff • Conducts research & development on samples from YNP	• For two years, advised the Park *pro bono* on its policy on partnerships with private companies • Assisted the Park with the negotiation of the CRADA with Diversa
MONETARY BENEFITS	• US$100,000 payable in 5 yearly instalments of US$20,000 • Undisclosed royalties of up to 10% upon commercialisation of a product derived from genetic resources sourced from the Park. Royalty rates are based on a sliding scale, depending on the end-use of the research results and the magnitude of sales.[102]	• Future profits from sales, in the event that a successful product emerges from the research based on YNP specimens.	• US$28,000 paid by the Park for assistance in negotiating the CRADA with Diversa.
NON-MONETARY BENEFITS	• Non-monetary benefits valued at US$75,000 per year, including: • Transfer of DNA extraction kits • Training in sampling techniques • Training in DNA fingerprinting techniques	• Access to genetic resources from YNP. • Right to develop commercial product from samples obtained earlier from YNP under the research specimen collection permit that prohibited use for commercial profit. • License to commercialise products derived from samples from the Park	• Notoriety.

[102] Appendix B, Cooperative Research and Development Agreement between Yellowstone National Park and Diversa, and personal communication with Preston Scott, WFED, 9 March 1998, and personal communication with Dr. Carolyn Ericson, Diversa, 22 April 1998.

IMPACT ON CONSERVATION

Prospecting activities in Yellowstone National Park involve two kinds of impact on conservation: first, the environmental impact of the activities themselves, and second, the manner in which the benefits that arise from the scientific research can contribute to conservation within the Park.

Environmental impact

In order to be granted a research permit within Yellowstone National Park, an applicant must demonstrate that the research activities will have no serious impact on the ecosystem. Applicants must show that the proposed activities are excluded from the environmental impact assessment process required by the National Environmental Policy Act.[103]

According to Diversa's Chief Executive Officer, water evaporates from a pool over a short period than would be removed during the collection of a water sample.[104] Similarly, the quantities involved in the collection of microbial samples are small. A scientist sampling from a bacterial mat may remove a plug of some 5 millimetres of material, and thus has less environmental impact than that caused by a single bison grazing in the area.[105] On the other hand, some ecosystems are sufficiently fragile that a single human footprint could damage them. Park scientists present during research activities advise visiting scientists on appropriate behaviour to protect the local environment.[106]

Support for conservation activities

One term of the Yellowstone-Diversa CRADA is that monies paid to Yellowstone National Park under the agreement with Diversa are to be paid into a special government account and earmarked for the Park's new Yellowstone Thermophiles Conservation Project.

The Yellowstone Thermophiles Conservation Project is a new initiative undertaken by Yellowstone National Park in cooperation with WFED, the Yellowstone Park Foundation, and the National Park Foundation. Intended to encourage cooperative scientific exploration of Yellowstone's thermal resources in ways that will capture benefits for Yellowstone and the conservation of its unique habitats, the Project will focus on th
ree areas of activity designed to generate support for strengthened resource conservation practices at the park: (1) microbial biodiversity conservation; (2) scientific research and data management; and (3) public outreach and education.[107]

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103 Personal communication, Bob Lindstrom, Yellowstone Center for Resources, 9 February 1998.

104 Personal communication, Terrance Bruggeman, Diversa, 17 February 1998.

105 Personal communication, Terrance Bruggeman, Diversa, 17 February 1998 and Bob Lindstrom, Yellowstone Center for Resources, 9 February 1998.

106 Personal communication, Bob Lindstrom, Yellowstone Center for Resources, 9 February 1998.

107 The information on the Yellowstone Conservation Project was kindly provided by Preston Scott, 9 March 1998.

The Yellowstone Thermophiles Conservation Project
Information provided by Preston Scott, WFED[108]

Microbial biodiversity conservation activities

Project activities will be designed to strengthen *in situ* thermal habitat conservation efforts as well as *ex situ* Yellowstone microbial culture collection development and maintenance. Specifically, Project-related conservation objectives at Yellowstone aim to:
(a) improve understanding about the origins and patterns of microbial biodiversity at Yellowstone to enhance habitat protection and resource management activities;
(b) develop and maintain a coordinated network of *ex situ* culture collections to complement the park's *in situ* habitat conservation activities that can provide specimen identification, authentication, and preservation services; and
(c) improve *in situ* and *ex situ* culture collection and preservation strategies.

Scientific research and data management

The Project will encourage expanded study of the Yellowstone's thermal habitats and promote activities to discover and describe new microbial forms, biochemical compounds, evolutionary branches and habitats. The Project also will explore development of an integrated database that includes habitat, geographical, biological and other key scientific information to benefit Yellowstone's microbial resource conservation and management practices. Specifically, Project-related scientific research and data management objectives at Yellowstone aim to: (a) improve understanding of spatial and temporal patterns of microbial diversity at Yellowstone; and (b) enhance appropriate methodologies to characterise, isolate, and identify microbial communities at Yellowstone.

Public outreach and education

The Project will place special emphasis on improving public awareness and appreciation of the value of national parks and the biodiversity they protect through publications, pamphlets, films and videos, presentations and media education, and in-the-field workshops and excursions. Through the promotion of cooperative partnerships that encourage scientific exploration in ways that will capture benefits for Yellowstone and the conservation of its unique habitats, the Yellowstone Thermophiles Conservation Project will explore innovative biodiversity management practices that can be adapted to meet the particular interests and needs of other national parks and conservation areas in the United States and abroad.

[108] Ibid.

CONCLUSIONS

Policy framework

In the light of the Convention on Biological Diversity, many countries are reviewing their legal, policy and administrative measures on access to genetic resources. This exercise often reveals that existing law relevant to access to genetic resources is unclear, incomplete or does not facilitate partnerships.[109] Law relating to the collection of, and research upon, specimens is often demarcated along sectoral lines (for example, forests, agriculture, fisheries), leaving gaps in the scope of law and policy related to access. These gaps are frequently geographical, by ecosystems, or by taxonomic category of genetic resource. An example of the last category is found in this case study, as U.S. legislation on national parks does not explicitly refer to microorganisms.

A further problem is that existing laws relevant to access to genetic resources were often introduced many years ago, and their objectives may relate more to the conservation of biodiversity than to ensuring prior informed consent for access and the fair and equitable sharing of benefits.

This case study reveals a specific aspect of this historical legacy of policy frameworks that were not originally designed to promote benefit-sharing. The U.S. statutes and regulations described in this case study that concern national parks, the protection of wildlife, technology transfer and public/private partnerships date from 1916 to 1986, and pre-date many international developments on access and benefit-sharing. One result is that the policy and legal framework for public bodies wishing to enter into agreements with companies that will develop commercial products from research on publicly owned genetic resources is open to interpretation.

One interpretation of this case study is that it is a positive example of a public body creatively interpreting the existing policy framework so as to allow access and benefit-sharing partnerships. Even if countries' existing laws and regulations do not explicitly address issues of access to genetic resources, commercialisation and benefit-sharing, they may provide an adequate structure within which to construct effective mechanisms for benefit-sharing and to control access so as to promote conservation. The position of the U.S. government that existing legislation would be sufficient for the U.S. to implement the access and benefit-sharing provisions of the CBD, should it become a party, follows this interpretation.[110] An alternative interpretation is that without clear, legislative guidance, public bodies endeavouring to establish access and benefit-sharing partnerships with companies cannot be confident that they are acting within their mandates, and may face criticism. The complaint filed against the Yellowstone National Park and the Department of the Interior illustrates the kind of criticism that may arise. From this, some would conclude that additional legal, policy or administrative measures on access and benefit-sharing are needed to clarify or alter the policy framework in such situations.

As this case has shown, there is room for uncertainty on this point. It is quite likely that similar uncertainties will exist elsewhere as national parks around the world contemplate arrangements

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[109] This assertion is based on opinion stated by representatives from countries represented at workshops held in Davao, Philippines in July 1997, Genting Highlands, Malaysia in August 1997, Cordoba, Spain in January 1998 and Chennai, India in February 1998, and also from personal communication with individuals working on access to genetic resources in the countries of the Andean Pact.

[110] see footnote 21, supra.

with private companies that intend to develop products for commercialisation. Such national parks would, therefore, benefit from clear law and policy on access and benefit-sharing issues. Take the case of the national parks in the United States, as illustrated by this case study. In order to enter into a CRADA, a U.S. National Park needs to be designated as a Federal laboratory. The degree of participation in the research conducted that is necessary for such a designation is not clear. Secondly, what is understood by "the sale or commercial use of natural products"[111] from a U.S. National Park is, again, open to interpretation. Informal exploration of this issue with the stakeholders interviewed for this case study reveals a difference of opinion as to what kind of activities would be prohibited.

It would appear to be relatively clear that the outright sale of genetic (and biological and mineral) resources from a U.S. National Park -- such as sales of seedlings of plants -- would infringe relevant legislation. The position with respect to the activities described in this case study, however, is disputed. Is it within the mandate of a U.S. National Park to enter into an agreement with a company that will isolate genes from specimens obtained from a U.S. National Park, transform the genes into other microbial hosts, screen these, and isolate and market the enzymes they express, or does this constitute "the sale or commercial use of natural products"? Yellowstone National Park and the Diversa Corporation believe these activities are allowed by the existing policy framework, while certain NGOs disagree.

Many collecting permits issued by the authorities regulating access around the world do not stipulate where a recipient of specimens is entitled to lodge them and on what terms. In some circumstances, this can provide a "loophole" whereby specimens collected under permits for non-commercial research are lodged in *ex situ* centres such as culture collections and then accessed without restriction from these centres and commercialised. The chain of events that led to this result in the case of Taq polymerase and the polymerase chain reaction, as described in this case study, is not likely to occur again at Yellowstone National Park. Yellowstone's Research Specimen Collection Permits restrict academic researchers to non-commercial uses only (unless the Superintendent has given his prior approval under a separate agreement), and prohibit researchers from passing specimens on to third parties, such as the American Type Culture Collection (ATCC), without the prior agreement of the Park. In addition, some *ex situ* collections, such as the ATCC, are now using material transfer agreements (MTAs). To avoid the negotiation and paperwork involved in a large number of similar, but individual MTAs involving the same parties, the ATCC could enter into umbrella Memoranda of Understanding between ATCC and institutions with whom it has frequent dealings, such as Yellowstone National Park. Together, legal mechanisms such as these should ensure that Yellowstone is entitled to be consulted prior to the development of commercial products, so that benefit-sharing arrangements can be established.

[111] 36 CFR 2.1 (c)(3)(v).

Objectives

The statutes governing the mandate of public bodies such as national parks may impose on them the challenge of reconciling a number of different duties when they enter into access agreements with private companies. For example, parks may be obliged to conserve ecosystems and the biological resources within them, on the one hand, and to allow researchers to obtain samples, on the other. They may be prohibited from commercialising park resources and yet be obliged to generate some revenue from research activities to lessen the burden on tax-payer.

The objectives of companies must also be balanced. Shareholders wishing companies to maximise profit may not wish them to share any more benefits than necessary with partners, and may not wish them to invest in conservation measures. At the same time, a minimum investment in benefit-sharing and conservation may be justified in purely commercial terms as a necessity for establishing partnerships to source genetic resources, and to protect ecosystems for future collecting activities. To a company such as Diversa, which sources genetic resources from extreme environments around the world, conservation of those environments is an important consideration. The company was anxious to ensure that monetary benefits received by Yellowstone National Park under the CRADA were dedicated to the Yellowstone Thermophiles Conservation Project.

Process for establishing the arrangements

Access and benefit-sharing arrangements operate best in a situation where all the major actors are in a relationship of trust. Transparency and accountability support such trust, but access to information such as the financial terms of a CRADA or inspection of laboratory reports and accounts may cause difficulties where companies require confidentiality or secrecy. Where access and benefit-sharing arrangements are made between private sector partners, clauses on confidentiality and on monitoring research can cover this. The situation is more complicated where one partner is a governmental body, if, as in the United States, there may be legislation providing a public right of access to such information.

Scientists and managers of protected areas entering into agreements with private sector companies frequently have neither the expertise nor the experience to conduct the type of negotiations over royalties, technology transfer, intellectual property rights, and the monitoring of research which are needed to secure a fair and equitable partnership. In this case, Yellowstone National Park recognised its need for expert help, and retained an NGO with legal experience to support the negotiations.

In order to ensure that all those with a stake in access and benefit-sharing activities (both at the policy setting and individual partnership level) accept government decisions on access agreements (and do not issue legal challenges to them), a participatory process that allows public comment prior to the introduction of new approaches to public resource management is likely to be important.

Given the difficulty of identifying the source of individual genes or isolated compounds ultimately used in products (and the added complication that the final products may include genetic resources from several countries), and given the small quantities of material that are often needed, in practical terms monitoring and enforcing access agreements is very difficult. This is all the more the case given that access to genetic resources is often encouraged, for academic reasons, so they may be

widely distributed and available from many sources. It is also particularly the case for microorganisms, as it may never be necessary to return to the source for more material if a product becomes interesting. Thus, while access agreements may be subject to legislation or based on binding contracts, their implementation relies to a large extent on trust between the partners. Despite this, there are some practical measures that can help partners monitor the use that is being made of the genetic resources in question. One example is inspection of laboratory notebooks that document developments in research.

From a company's perspective, an important element of the negotiation of an access and benefit-sharing agreement is how long it takes, how smoothly it proceeds, and the ability to be confident, finally, that agreement has been reached definitively.[112] Companies are frequently concerned that negotiations on access and benefit-sharing will delay product discovery and development.[113] If government authorities regulating access to genetic resources are to respond to such concerns on the part of business, they need to coordinate the negotiation and review of agreements between different departments of government. It is notable in this case that negotiations proceeded over a period of years, and that periods for review by government were voluntarily extended by the company more than once. Furthermore, the terms of the original CRADA between Diversa and Yellowstone National Park, although approved in August 1997 by senior government officials, were amended in April 1998 in order to take into consideration comments by other government representatives.

Inputs

Protected areas can contribute more than access to genetic resources to access and benefit-sharing partnerships. In the case of Yellowstone National Park, staff who are familiar with the biodiversity in the Park can provide expertise and information that can assist in sampling genetic resources, and also provide information that can help in the selection of locations for sampling.

Benefits

Non-monetary benefits shared by companies (such as know-how and training) need not be linked to the research conducted by the company on the samples accessed. In this case study, the Diversa corporation helped Park staff to detect Brucellosis, work which was unconnected to the company's product discovery and development programmes, but useful to the Park.

Up-front benefits may be more useful than long-term ones, given the vagaries of product development. However, in this case study, the up-front benefits are creditable against future royalties, not in addition to them.

One factor that managers of protected areas will need to take into consideration is the cost of entering into partnerships with companies. The value of specified (and thus certain) short-term benefits, and of long-term benefits that will arise only in the event that product development is successful, need to be set off against the costs to the protected area of entering into such

[112] see ten Kate, K. and Laird, S., 1997. *Placing Access and Benefit-Sharing in the Commercial Context: A Study of Private Sector Practices and Perspectives*. RBG, Kew and WRI. Unpublished.
[113] Ibid.

arrangements, such as the costs of hiring legal expertise to negotiate the agreement and defend it against any law suits, staff time involved in accompanying collectors to obtain samples, any potential environmental damage, and - though this potential cost is less easily quantified - any effect on the reputation of the protected area, and thus on public relations, through entering into agreements with commercial partners.

Conservation

There are links between conservation and access and between conservation and benefit-sharing.

The links between conservation and access relate to sustainable sourcing. Permits should be granted subject to a commitment to procedures for ensuring that sampling techniques do not damage the ecosystem or genetic resources. Sourcing of microorganisms for biotechnology applications often has less environmental impact than, for example, sourcing plant materials for the phytomedicine industry, as the quantities required in the former are small, and generally only require one collection, whereas the latter generally needs ongoing supplies of large quantities of raw material.

However, while genetic engineering and biotechnology may reduce the environmental impact of collecting activities through reducing the quantity of material sampled, if genetically modified products result from the research and are released into the environment, this may give rise to other issues related to conservation, such as biosafety.

The links between conservation and benefit-sharing are that access activities will generally only make a positive contribution to conservation (as opposed to just minimising the impact of access) if specific provision is made in access agreements to require some benefits to be dedicated to conservation. In this case, any funds received by YNP will be dedicated to conservation, research and outreach activities.

Companies entering into access and benefit-sharing partnerships with public bodies such as agencies responsible for managing protected areas like to see that monetary benefits are dedicated to conservation, and are not simply swallowed up into general government coffers. Since mechanisms to achieve this may not exist already, some public bodies may need to consult with higher authorities and put in place mechanisms to ensure that monetary benefits received are paid directly into accounts for use in local conservation activities.

Lessons Learned

One lesson that can be learned by public bodies from this case study is the need to establish clear procedures for public comment prior to embarking on a new kind of partnership that may result in the development of commercial products from research on publicly owned genetic resources. Such a consultation should involve not only the academics, companies and NGOs who are likely to be directly involved in bioprospecting activities themselves, but those who represent environmental, biosafety and local community and users' groups.

Replicability

Yellowstone National Park has taken the lead in exploring the possibilities of research partnerships with private companies, in response to the request by the Director of the National Park Service. The Park has already been contacted by several other U.S. National Parks, seeking advice about entering into research agreements with private companies.

Protected areas around the world may wish to seek clarification of law concerning microorganisms, "commercialisation", public review and access to information prior to entering into research partnerships with commercial enterprises. A primary consideration is whether the existing policy framework is adequate for such partnerships, or whether it would first be necessary to introduce new enabling or clarifying legislation. It might be useful for the appropriate government authorities to develop guidelines to help agencies managing protected areas and others controlling access to genetic resources to understand how to proceed in the future.

ANNEX:
CURRENT INVENTORY OF NEWLY DESCRIBED MICROORGANISMS FIRST ISOLATED AT YELLOWSTONE NATIONAL PARK[114]

Acidothermus cellulolyticus (Citation: Int. J. Syst. Bacteriol. 36:435-443 (1986).)

Alicyclobacillus acidocaldarius (*Bacillus acidocaldarius*) (Citation: J. Gen. Microbiol. 67:9-15 (1971). Produces a restriction endonuclease.)

Bacillus sp. (Thermal spring sediment) (Citation: Appl. Microbiol. Biotechnol. 33:340-344 (1990). Degrades pullulan.)

Chloroflexus aurantiacus (Citations: Description (Arch. Microbiol. 100: 5-24 (1974); sulfide oxidation (J. Bacteriol. 122:782-784 (1975); lack of diazotrophy (J. Gen. Microbiol. 132:2469-2473 (1986)).)

Chromatium tepidum (Citations: Characterization (Science 225: 313-315 (1984); type strain (Int. J. Syst. Bacteriol. 36:222-227 (1986)).)

Methanobacterium thermoautotrophicum (Citation: Characterization (J. Bacteriol. 143:432-440 (1980)).)

Moorella thermoautotrophica (*Clostridium thermoautotrophicum*) (Citations: Curr. Microbiol. 5:255-260 (1981); type strain (Int. J. Syst. Bacteriol. 32:384-385 (1982); Int. J. Syst. Bacteriol. 44:812-826 (1994).)

Rhodopila globiformis (Citations: Arch. Microbiol. 100:197-206 (1974); type strain (Int. J. Syst. Bacteriol. 30:225-420 (1980); Int. J. Syst. Bacteriol. 34:340-343 (1984).)

Sulfolobus acidocaldarius (Citations: Type strain (Int. J. Syst. Bacteriol. 30:225-420 (1980). Produces citrate synthase (Syst. Appl. Microbiol. 6:119-124 (1985)); and restriction endonuclease *SuaI* (FEBS Lett. 192:57-60 (1985)).)

Synechococcus sp. (*Synechococcus lividus*) (Citations: Taxonomy (Bacteriol. Rev. 35: 71-205 (1971); J. Gen. Microbiol. 111:1-61 (1979)).)

Thermoanaerobacter acetoethylicus (*Thermobacteroides acetoethylicus*) (Citations: Methanogenesis (J. Bacteriol. 143: 432-440, 1980); type strain (Arch. Microbiol. 128:365-370 (1981); Int. J. Syst. Bacteriol. 33:672-674 (1983); Int. J. Syst. Bacteriol. 43: 857-859 (1993)).)

Thermoanaerobacter brockii (*Thermoanaerobium brockii*) (Citations: Type strain (Int. J. Syst. Bacteriol. 33:672-674 (1983); Int. J. Syst. Bacteriol. 43:41-51 (1993)).)

Thermoanaerobacter ethanolicus (*Clostridium thermohydrosulfuricum*) (Citations: Produces thermostable pullulanase and glucoamylase (Appl. Environ. Microbiol. 49:1168-1173 (1985); U.S.

[114] Information provided by Preston Scott, WFED, 9 March 1998.

Pat. 4,604,352); and ethanol from starch (U.S. Pat. 4,604,352). Taxonomy (Int. J. Syst. Bacteriol. 43:41-51 (1993)).)

Thermoanaerobacter thermohydrosulfuricus (*Clostridium thermohydrosulfuricum*) (Citations: Production of thermostable beta-amylase, glucoamylase and pullulanase during the conversion of starch to ethanol (U.S. Pat. 4,737,459).)

Thermoanaerobacterium thermosulfurigenes (*Clostridium thermosulfurigenes*) (Citations: Type strain (Int. J. Syst. Bacteriol. 33:896-897 (1983); Int. J. Syst. Bacteriol. 43:41-51 (1993)). Production of thermostable extracellular beta-amylase (Appl. Environ. Microbiol. 49:1162-1167 (1985); U.S. Pats. 4,647,538 and 4,604,352); ethanol from starch (U.S. Pats. 4,647,538 and 4,604,352); and pectin methylesterase and polygalacturonate hydrolase and conversion of thiosulfate to elemental sulfur (U.S. Pats. 4,572,898 and 4,721,676).)

Thermodesulfobacterium commune (Citations: Type strain (Int. J. Syst. Bacteriol. 45:197-198 (1995); J. Gen. Microbiol. 129:1159-1169 (1983). Produces glycerol ethers (Syst. Appl. Microbiol. 4:1-17 (1983)).)

Thermodesulfovibrio yellowstonii (Citations: Type strain (Int. J. Syst. Bacteriol. 44:595 (1994); Arch. Microbiol. 161:62-69 (1994)).)

Thermoleophilum album (Citations: Growth on long-chain hydrocarbons (FEMS Microbiol. Lett. 3:81-83 (1978). Characterization (Int. J. Syst. Bacteriol. 36:13-16 (1986); Arch. Microbiol. 137:286-290 (1984)).)

Thermoleophilum minutum (*Thermoleophilum album*) (Citations: Type strain (Int. J. Syst. Bacteriol. 36:13-16 (1986)). Characterization (Arch. Microbiol. 137:286-290 (1984)).)

Thermomicrobium roseum (Citations: Type strain (Int. J. Syst. Bacteriol. 30:225-420 (1980); Int. J. Syst. Bacteriol. 23:28-36 (1973)). Cell wall composition (Can. J. Microbiol. 26:556-559 (1980)).)

Thermus aquaticus (Citations: Type strain (Int. J. Syst. Bacteriol. 30:225-420 (1980); J. Bacteriol. 98:289-297 (1969)).)

Thermus sp. (Citations: Inducible for a thermostable beta-galactosidase on lactose and galactose (J. Ulrich, personal communication).)

Thermoanaerobacterium xylanolyticum (Citation: Type strain (Int. J. Syst. Bacteriol. 43:41-51 (1993)).)

Thermoanaerobacter ethanolicus (Citations: Type strain (Int. J. Syst. Bacteriol. 32:384-385 (1982); Arch. Microbiol. 128:343-348 (1981)). Produces alcohol dehydrogenases (Appl. Environ. Microbiol. 54:460-465 (1988)). Production of ethanol from cellulose (U.S. Pat. 4,292,406).)

Unidentified bacterium (Citation: ATCC 55712)